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PARTIAL PANCREATECTOMY IN CHRONIC SPONTANEOUS HYPOGLYCÆMIA

WITH A REVIEW OF THE CASES OF HYPOGLYCÆMIA SURGICALLY TREATED

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THE specific treatment of diabetes, or hypoinsulinism, with insulin has inevitably led to a knowledge of its counterpart, hyperinsulinism. Indeed, it is said that certain investigators long preceded Banting and Macleod in the discovery of a pancreatic substance so potent in its correction of diabetes that it had to be abandoned mainly because of the convulsive seizures that attended its administration.

Hyperinsulinism produces a train of symptoms, the severity of which is directly proportional to the insulin excess and the resulting hypoglycæmia. Three surgical conditions have been recorded in the literature as being responsible for this insulin excess:

1. Metastasizing tumors or carcinomata of the islets of Langerhans which, contrary to the usual carcinoma of secreting glands, have retained their normal property of producing insulin.

2. A benign tumor or adenoma of the islets of Langerhans, comparable to an adenoma of the thyroid.

3. An overactivity of an otherwise normal-appearing pancreas, comparable, as pointed out by Wilder, to hyperthyroidism due to hyperplasia.

Within the last 8 years all three conditions have been subjected to surgical intervention, with amelioration and, in a few cases, complete cure of the disease. The following brief summaries of these recorded surgical cases illustrate the characteristic symptoms accompanying this rather recently recognized clinical entity:

CASE 1. (Mayo Clinic.) Carcinoma of the islands of the pancreas. Hyperinsulinism and hypoglycæmia. Wilder, Allan, Power, and Robertson. J. Am. M. Ass., 1927, lxxxix, 348.

A physician, aged 40, 18 months before admission to the Mayo Clinic began having sudden attacks of faintness and weakness, with paræsthetic numbness of the tongue and lips. As time passed these attacks occurred more frequently and were more severe, producing greater weakness, profuse perspiration, and trembling. They came when meals were delayed or if unusual exertion was undertaken, and the patient himself discovered that he could prevent them by eating between meals and by taking sweet drinks. The first attack resulting in collapse came in November, 1925. The patient had been operating later than usual and, being overtaken by weariness, was soon mentally confused and collapsed in a stupor. Attendants thought he had lost consciousness, but he was able to swallow an egg-nog, which an assistant gave him, and in a few minutes had completely revived.

As time passed, the tendency to hypoglycæmia increased so that the interval between the patient's taking food had to be decreased and it became necessary for his wife to watch when the patient slept and put candy into his mouth at the first sign of unusual behavior. For the purpose of studying the hypoglycæmic reaction, after the mixed noon meal

of October 31, sugar was withheld. The patient remained in bed under constant observation. The systolic blood pressure was 110 and the diastolic 60. The first symptoms appeared 3 hours and 20 minutes after the meal, when the blood sugar had fallen to 0.055 grams per 100 cubic centimeters. There was a sense of apprehension and depression, with vague paræsthesia. Fifteen minutes later, perspiration and tremor were noted. At 4 hours the blood sugar had fallen to 0.036 grams per 100 cubic centimeters, the face twitched, speech was incoherent, and the systolic blood pressure was elevated to 134 while the diastolic remained at 60. At 4 hours and 15 minutes the blood sugar reached 0.027 grams per 100 cubic centimeters; the patient was stuporous and no longer able to speak, tossing about with irregular, convulsive jerkings that affected the entire body. Fifteen grams of dextrose were fed by mouth, and in 10 minutes rational conversation was resumed. The blood sugar was 0.065; the systolic blood pressure was 122, and the diastolic 48.

In this instance the administration of epinephrin had little effect, as compared with experiences in other cases. One milligram of epinephrin was administered at a time when the patient was beginning to manifest symptoms of hypoglycæmia and when the blood sugar was 31 milligrams per 100 cubic centimeters. The symptoms were not affected and sugar had to be given 4 minutes later to prevent collapse. Pituitrin injected when the blood sugar was low caused symptoms to appear, and 40 minutes later a second injection was made. Sugar was required within 5 minutes after the second injection.

At operation, December 4, 1926, a hard firm nodular pancreas was felt and several nodules in the liver. At his death a month later a carcinoma of the islands of Langerhans with metastases to the liver was found. The carcinomatous tissue from the liver yielded at least 40 units of insulin for each 100 grams. It is of interest that before operation the ingestion of 20 grams of dextrose an hour was necessary to avoid symptoms of hypoglycæmia, whereas just before death 1000 grams of sugar were required daily.

Case 2. (Union Memorial Hospital, Baltimore.) Resection of the pancreas (Finney and Finney). Ann. Surg., 1928, lxxxviii, 584.

A woman, aged 53 years, entered the hospital in December, 1927, with the complaint of spells of confusion, with mental lapses and strange behavior. Her illness had begun 4 years previously, coincident with her menopause. At first the attacks were slight and infrequent. It was noted that she would seem dazed, could not concentrate or think clearly, and sometimes would "see double." The attacks at that time would be of but a few minutes' duration, with no after effects. After a year and a half, she became alarmed about her health, and went to Europe for a rest. During the year spent there, there were about six or eight attacks. They usually occurred before breakfast, but had not as yet come to be definitely associated with the taking of food. Any alarm or trouble might precipitate an attack. Once or twice she fell while walking, but was conscious of no dizziness, and was able to arise immediately and continue. During the 18 months preceding admission the attacks had increased rapidly both in number and severity, until they had become daily in occurrence, usually before breakfast.

A typical attack was described as follows: diplopia and great difficulty in properly focusing her eyes were often the initial symptoms. Then the head began to jerk unsteadily and roll from side to side. At the height of the attack, she screamed and threw herself violently about. There was at times some frothing at the mouth. There had never been any biting of the tongue, or other physical injury during an attack, nor any loss of sphincteric control. Everything that occurred during the attack was hazily remembered by the patient afterward. She felt exhausted, both mentally and physically. The attacks lasted from 15 minutes to several hours. Upon one occasion she said she was semi-conscious for a whole day. The most interesting feature about these attacks was that they were aborted in a few minutes if, at the first warning of their approach, the patient took a few mouthfuls of shredded wheat biscuit and cream. From September to December, 1926, while under treatment at a sanatorium, on forced feedings and bromides, she had no seizures at all.

A number of blood sugar estimations had been made during the period of her illness: September, 1925, 134 milligrams per 100 cubic centimeters; September, 1926, 41 milligrams per 100 cubic centimeters; October, 1926, 79 milligrams per 100 cubic centimeters; May, 1927, 30 milligrams per 100 cubic centimeters. The basal metabolic rate was −9 and −6 on two examinations. Other laboratory examinations were practically normal.

Ten units of insulin were given hypodermically, with the immediate production of an attack. From this attack she recovered with equal rapidity, following the intravenous injection of a glucose solution. On another occasion, 10 units of insulin were given intravenously, together with 20 grams of glucose, without the production of an attack. At the time of these experiments, the blood sugar was at a normal level before the insulin was given. During the attack, it was very low, from 20 to 30 milligrams per 100 cubic centimeters. Immediately after recovery, following the injection of the glucose, it had again become normal. On the other hand, at another time, while in the fasting state, with a very low blood sugar, a hypodermic injection of 10 minims of adrenalin prevented the occurrence of an attack, and an hour later, the blood sugar was found to be normal. The same result was obtained by the injection of pituitrin, hypodermically and, also, though less promptly, by the use of pituitrin intranasally. Ephedrin solution had no effect whatever in warding off an attack.

At operation, December 3, 1927, the pancreas and liver seemed normal in size, shape, and consistency.

Owing, however, to the persistent, unexplained hypoglycæmia, it was decided to resect a portion of the pancreas. Accordingly, beginning at the tail, the pancreas was mobilized and dissected out of its bed until approximately two-thirds of it had been freed. When as much of the pancreas had been mobilized as it seemed wise to remove—approximately 22.5 grams—the body of the gland was divided by a V-shaped incision, and the resulting flaps of pancreatic tissue were brought together and sutured with continuous plain catgut, which effectually covered in all the raw surfaces and controlled the oozing therefrom. On microscopic section the removed tissue was apparently normal pancreas.

After operation the blood sugar varied from 45 to 70 milligrams per 100 cubic centimeters. From December 12 to December 20, the patient had light attacks almost daily, usually the first thing in the morning; occasionally at other times during the day. None of these attacks were severe, nor did they progress beyond the point of uncomfortable sensations with a peculiar staring expression of the eyes, facial grimacing, and general restlessness. At all times, the administration of a few drams of glucose immediately aborted an attack.

On the eighteenth day after operation there was a severe attack which subsided promptly on taking a few mouthfuls of shredded wheat, sugar, and milk. It was followed by a crying spell, and the patient was very much depressed for the rest of the day. Vena-puncture was done during the attack and the blood sugar was 50 milligrams. It would appear that not sufficient pancreas had been removed to control adequately the hyperinsulinism, or a small adenoma had been overlooked.

CASE 3. (Stanford University Hospital.)

A man, 31 years old, entered the hospital on May 6, 1928, with the complaint of "spells of unconsciousness." His past history was unimportant. His illness dated back one and a half years when on several occasions he was compelled to quit his work late in the morning because of pronounced weakness. He recalls one occasion when he became "groggy" but did not lose consciousness. About one year ago after a morning's work in the field and while returning to the house his legs became quite weak causing him to stagger. This was associated with mental confusion and disorientation, followed by collapse and loss of consciousness. He was given a cup of hot chocolate following which he recovered immediately. Similar attacks occurred at infrequent intervals usually after several hours of hard work, and they were always relieved by taking food. On one occasion after attending a dance he failed to awaken in the morning and could be aroused only after food had been administered.

At the onset of the illness the attacks occurred at intervals of 1 to 2 months but after 4 months they occurred once in every 2 or 3 weeks. It was about this time that the patient associated the attacks with the need for food and thereafter he was able to abort or prevent them by eating. As time passed the attacks gradually became more severe and more frequent, and on one occasion while in Central America he was placed in a hospital under observation. Here he was told that he had convulsions accompanying the attacks. He returned to the United States and entered Lane Hospital for treatment.

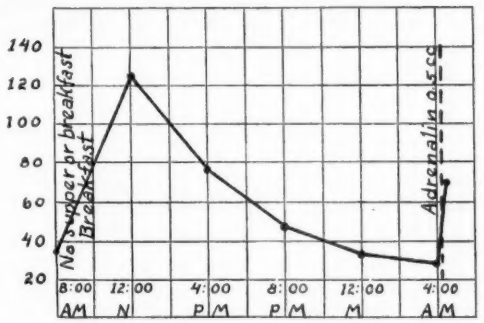

Fig. 1. The course of the blood sugar during a 20 hour fast. Supper was omitted the evening before with breakfast on the day of the fast. The vertical line represents the milligrams of sugar per 100 cubic centimeters of blood. Note that a blood sugar of 35 milligrams rose to 74 milligrams following the injection of 0.5 cubic centimeter of adrenalin.

The physical examination on admission revealed no abnormalities. The Wassermann reaction was negative. The gastric acidity as tested by the alcoholic meal was normal. The spinal fluid showed three cells, negative Nonne and Noguchi reactions, the colloidal gold curve was normal, and the Wassermann positive in the first two dilutions. The basal metabolic rate was −20 per cent. In view of the patient's history it was decided to observe his reaction to starvation. He was deprived of his evening meal. The following morning at 8:30 he was quite pale, sweating profusely, tossing about in bed, laughing, giggling, and talking incoherently. He refused to answer questions. The eyes were staring or tightly closed, the pupils were dilated, the pulse was rapid but not alarmingly so. As he refused to eat, an attempt was made to pass a stomach tube, against which he fought viciously. He was finally left to himself and about 3 hours later when his tray was brought he roused sufficiently to take nourishment and within 10 minutes he was again normal, stating he remembered nothing of the morning's episode.

The blood sugar during the attack was found to be 38 milligrams per 100 cubic centimeters. The blood sugar was then determined at intervals of 4 hours over a period of 24 hours. The patient was deprived of supper the evening before and given only breakfast on the day of the test. The results are shown in Figure 1. On the morning of the test, after 20 hours of starvation, the blood sugar was 36 milligrams per 100 cubic centimeters. At this time he was conscious but definitely confused mentally. Following breakfast he was perfectly normal and at

12 noon the blood sugar was 128 milligrams per 100 cubic centimeters. During the day the blood sugar gradually fell and at 4 a.m. he was unconscious, lying quietly in bed, sweating profusely, pale, his eyes rolling aimlessly about. The blood sugar at this time was found to be 32 milligrams per 100 cubic centimeters. After 0.5 cubic centimeter of a 1:1000 dilution of adrenalin hydrochloride, he recovered almost immediately and a blood sugar taken at this time was found to be 71 milligrams per 100 cubic centimeters. Two days later a sugar tolerance test was made. The fasting blood sugar was 60 milligrams per 100 cubic centimeters. One hundred grams of glucose were given by mouth and at no time for the succeeding 3 hours did the blood sugar reach 100 milligrams per 100 cubic centimeters, remaining constantly at about 80 milligrams per 100 cubic centimeters.

The patient was placed on a quantitative diet with a glucose equivalent of 401 grams including intermediate nourishment at 10 a.m., 3 a.m., and 11 p.m. During the next 2 days he felt fine and had no attacks. While he was on this high carbohydrate diet blood sugar estimations were done over a period of 24 hours. In spite of the high caloric diet and the frequent feedings the blood sugar never reached 100 milligrams per 100 cubic centimeters and the morning blood sugar after 9 hours of fasting was only slightly above 50 milligrams per 100 cubic centimeters.

In view of the low basal metabolic rate the effect of thyroid extract was tried. He was given 5 grains of Armour's thyroid extract daily and at the end of 8 days the basal metabolic rate was −3 per cent. During this time he remained on the same quantitative diet equivalent to 401 grams of carbohydrate. A series of blood sugar estimations made at this time when compared with those prior to starting thyroid were slightly higher during the day but the net result during the early morning hours was practically the same. In view of the fact that there was no appreciable alteration in the blood sugar or general condition administration of thyroid was discontinued.

In view of the probability that this patient was suffering from hyperinsulinism due to a tumor of the islands of Langerhans (pancreisles),[1] he was advised to have an exploration of the abdomen, but this advice was refused and he was dismissed from the hospital on May 28, 1928.

The patient remained at home for a month, and felt fine on a diet with a carbohydrate equivalent of 355 grams including nourishment upon retiring. At the end of this time he returned to work. On the morning of the third day he failed to awaken and was roused only after being given nourishment. From this time on he had frequent repeated attacks following the slightest physical exercise. After further consideration he finally consented to operation, and he again entered the hospital August 8, 1928.

[1] The increasing literature on disease of the islets of Langerhans suggests that the simpler name "pancreisles" be used to designate this portion of the pancreas.

A series of blood sugar determinations done after 3 days on the former diet with a carbohydrate equivalent of 401 grams were practically identical with those done on the previous entry. His hourly consumption of carbohydrate was determined before operation so that a postoperative hypoglycæmia might be avoided. A duodenal tube was passed and at fluoroscopy 4 hours later, the bucket was seen in the duodenum. He was given 25 grams of glucose per hour through the tube. A blood sugar determination at the end of 5 hours was 95 milligrams per 100 cubic centimeters, at the end of 9 hours it was 88 milligrams per 100 cubic centimeters. Apparently 25 grams per hour was just below his carbohydrate consumption.

A laparotomy performed by Holman on September 1, 1928, revealed a normal appearing stomach, liver, and gall bladder. The pancreas was exposed by dividing the gastrocolic omentum. It appeared normal and, although quite firm, no masses or abnormal densities were encountered on palpation. It did not appear abnormally large. The inferior border of the tail and body were easily mobilized, but the splenic artery and vein along the upper border with their numerous tributaries entering the pancreas effectively prevented the freeing of the upper border. Accordingly, the splenic vessels were deliberately included in mass ligatures placed through the pancreatic tissue about 8 centimeters apart, and the intervening pancreas was removed. If the opportunity to resect a pancreas again presents itself I should be tempted to mobilize the spleen and remove it together with the pancreas, thus permitting complete removal of the tail and as much of the body as was thought necessary without the necessity of saving the splenic artery and vein. The stumps of the pancreas were covered with adjacent peritoneal folds, the rent in the gastrocolic omentum sutured, and the abdomen closed in layers without drainage. During the operation 3,000 cubic centimeters of a 5 per cent glucose solution was administered subcutaneously, and immediately after operation 500 cubic centimeters of a 5 per cent glucose solution was given intravenously.

Microscopic study of the pancreas revealed no obvious anatomical abnormalities.

The immediate postoperative course was uneventful. Immediately after operation the blood sugar measured 450 milligrams per 100 cubic centimeters with a rapid fall during the first few hours to 200 milligrams per 100 cubic centimeters. During the 4 days following operation it gradually fell to 80 milligrams per 100 cubic centimeters where it remained for about one week with another fall to 40 to 50 milligrams per 100 cubic centimeters. At this time he again began to have slight mental confusion. On the thirteenth day after operation he complained of a fullness in the abdomen, and 3 days later a mass appeared in the epigastrium which was thought to be a collection of pancreatic fluid. On September 22 the abdomen was reopened through the upper part of the previous operative wound and 1,500 cubic

centimeters of a thick grayish fluid removed containing numerous necrotic bits of tissue which microscopically proved to be pancreas. It was obvious that the pancreas included in the transfixion ligatures had been digested away, thus increasing considerably the amount of pancreas removed. Five small cigarette drains were introduced into the cavity, and the abdomen was closed. During the next few days there occurred a profuse drainage of thin fluid containing many bits of necrotic tissue. This drainage gradually lessened and he was discharged from the hospital on October 6.

Following the second operation the fasting blood sugar remained low, and as he continued to be on the verge of a hypoglycæmic reaction each morning, it became necessary to give nourishment during the night. After his return home he continued to give evidence of a glycopenic state in spite of nourishment during the night. On October 20, 1928, a sugar tolerance test was again done and on comparing it with that before operation it was found that the blood sugar reached a higher peak, but that at the end of 3 hours it was again back to 50 milligrams per 100 cubic centimeters.

The effect of pituitrin upon the blood sugar was then studied. A sugar tolerance was done in the same manner as before except that pituitary extract (B. W.) 0.5 cubic centimeter was given hypodermically 15 minutes after the 100 grams of glucose. In Figure 2 is plainly seen that the peak value is much higher but the fall more rapid, so that at the end of 2 hours, 45 minutes, the values are practically the same. He was then placed on pituitary extract (B. W.) 0.3 cubic centimeter 15 minutes after breakfast and dinner, but as no beneficial effect on the blood sugar values resulted the pituitrin was soon discontinued.

Although complete relief from previous symptoms was not obtained immediately it was soon apparent that definite improvement had been effected. In April, 1929, he reported his hypoglycæmic symptoms had been helped considerably. He was able to go through the day's work without leaving it to eat. In June, 1930, a series of tests at the Virginia Mason Hospital in Seattle showed the blood sugar at a higher level, and he reported himself much improved.

It is apparent, however, that in a future comparable situation the removal of more pancreas would be indicated. A normal spleen is easily removed and to avoid any difficulties of hæmorrhage from the splenic artery and vein, it would appear desirable to mobilize the spleen and the tail of the pancreas well up to the body making an attempt to reduce the size of the pancreas by two-thirds or three-fourths. If the analogy between hyperthyroidism and hyperinsulinism is applicable, as suggested by Wilder, certainly a major portion of the pancreas must be removed to correct the hyperinsulinism. Moreover, it would appear advisable also to introduce temporary drains to the operative bed to afford a removal of pancreatic secretion from the transfixed stump of pancreas, thus avoiding the complication experienced in this instance.

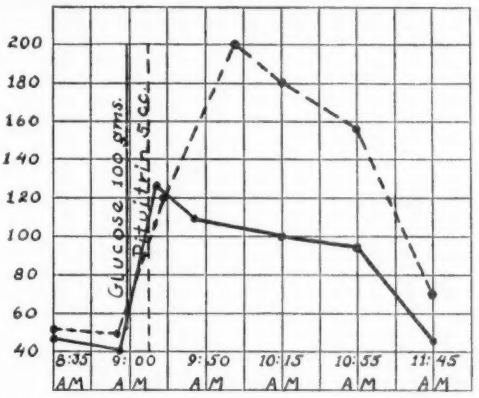

Fig. 2. Comparison of blood sugar curves after 100 grams of glucose with and without pituitrin. Solid line represents the blood sugar without pituitrin, the dotted line with pituitrin. The vertical line represents the milligrams of sugar per 100 cubic centimeters of blood.

CASE 4. (Mayo Clinic.) Hyperinsulinism by Allan. Arch. Int. Med., 1929, xliv, 65.

A farmer, aged 52 years, came to the Mayo Clinic in August, 1928, because of attacks of weakness and stupor which had occurred at intervals for more than 2 years. On many occasions he had lost consciousness and had had convulsions. He noted that the attacks were most likely to occur if he had gone without food for several hours, or if he undertook any exertion. He found that eating would relieve or prevent the symptoms, so he formed the habit of taking food at frequent intervals. As time went on, the patient had to take larger amounts of food at shorter intervals. For several months before admission, he had been obliged to eat at bedtime and during the night. He was unable to work; slight exertion, such as mowing his lawn, often precipitated attacks. Even when resting, failure to take sufficient food resulted in attacks several times a week.

Investigation showed that when food was withheld, there was a gradual fall in the level of the blood sugar. If it fell below 0.06 per cent, the usual symptoms of hypoglycæmia appeared. The lowest amount of blood sugar observed was 0.04 per cent. To prevent hypoglycæmia, food with the equivalent of 500 grams of dextrose each day was required, lunches being given between meals and three times during the night. The injection of epinephrin hydro-

chloride caused a rise in blood sugar, and temporary relief of symptoms. Solution of pituitary had a similar influence, although it was less powerful.

At operation, September 12, 1928, the pancreas and neighboring organs appeared normal. The tail of the pancreas and part of the body were resected. The portion removed weighed 14 grams. Microscopic examination did not show visible abnormality.

Following operation, slight improvement was noted for a time, but in November, 1929, the patient described his condition as being similar to that before operation. He was obliged to eat regularly. between meals, and once during the night.

CASE 5. (Toronto General Hospital.) Dysinsulinism. Convulsions and coma due to islet cell tumor of the pancreas, with operation and cure. Howland, Campbell, Maltby, and Robinson. J. Am. M. Ass., 1929, xciii, 674.

The patient, aged 52 years, complained in September, 1922, of extreme exhaustion and attacks which were described as of minor and major character: extreme faintness usually preceded the attack in which the patient became dazed, looked fatuous, and was restless. These minor attacks occurred so often at the table that it was suggested that the smell of food was a stimulus to insulin release. In the major attack, which might be preceded by diplopia or by a feeling of numbness in the legs, the mental confusion was deeper; she had to be placed in bed, where the grimacing became very evident; one could not arouse her although the eyes might be open; her appearance was in some degree similar to that of an intoxicated person. Then the convulsion would commence with violent kicking, and tossing about of the arms and body, there being excessive secretion of saliva and incontinence of urine and fæces. No degree of stimulus appeared to rouse her until the onset of sweating and vomiting, and then, soaking wet with perspiration, the patient would return to consciousness. Occasionally the patient became drowsy and slipped quietly into a coma to wake up later without any realization of the lapse of time or of events taking place during the comatose period. Following two of the severe seizures, the left arm and leg became paretic; and, while this lasted only a few hours in the first attack, in the later one it remained some days, associated with thick, slurring speech.

Complete neurological examination was always negative. The blood sugar during a typical attack ending in unconsciousness was 0.04 milligrams per 100 cubic centimeters, and prompt relief was obtained by the administration of dextrose intravenously. A high carbohydrate diet plus three-fourths pound sugar daily was required to keep her in a normal state. Five cubic centimeters of epinephrin restored the blood sugar from 40 milligrams per 100 cubic centimeters of blood to 110 milligrams within one hour. Solution of pituitary administered at a time when the blood contained 195 milligrams of sugar per 100 cubic centimeters blood caused the sugar to drop to 145 milligrams per 100 cubic centimeters.

At operation in March, 1929, a small tumor, 1.5 centimeters in diameter, was removed from the midportion of the pancreas, which was without capsule, and composed of masses of epithelial cells of the islet of Langerhans type, diagnosed as carcinoma. Insulin was recovered from this tissue. No attacks occurred subsequent to the operation and the patient was at least temporarily cured.

This case constitutes the first successful treatment of an adenocarcinoma of the islands of Langerhans recorded in the literature.

CASE 6. (Barnes Hospital, St. Louis.) Hyperinsulinism from B-cell adenoma of the pancreas. Carr, Parker, Grove, Fisher, and Larimore. J. Am. M. Ass., 1931, xcvi, 1363.

A youth, aged 19 years, entered the hospital January, 1930, because of convulsive seizures diagnosed as epilepsy. About 1 year previously he had his first attack of unconsciousness in which his behavior was abnormal, and of which he remembered nothing. Other attacks followed at increasingly shorter intervals and became more profound and prolonged, and at the time of admission they were occurring almost daily, usually in the late morning, and especially during times of stress from school duties.

The attacks varied in severity but were essentially the same in character. They began with a feeling of "queerness inside," a sense of hunger and anxiety. He became confused but would continue awkwardly in whatever he was doing. On one occasion, he drove for 45 minutes over busy city streets and had no remembrance of doing so. From confusion the attacks progressed into a stupor with profuse perspiration, slight cyanosis and, at times, more or less muscular movement. Recovery would occur spontaneously after a few hours and he was then tired and ravenously hungry. Food would promptly relieve the residual drowsiness. He had observed that an attack could often be aborted by eating candy, and his mother had discovered that, if she could get him to take a few sips of sweetened tea at the onset of an attack, he would sometimes arouse sufficiently to finish the cup, and the attack would be much milder. The anamnesis did not reveal any disorder of bodily functions between the attacks or otherwise during them.

Physical examination revealed normal condition in all essential details. During an attack of unconsciousness in the hospital, the blood sugar determination showed 44 milligrams per 100 cubic centimeters. Five grams of dextrose introduced intravenously brought a prompt return of consciousness. For a time a diet rich in carbohydrates caused almost complete relief of symptoms but by October a definite increase in severity of symptoms prompted surgical intervention. At the operation on October 22, 1930, the pancreas was exposed through the gastrocolic omentum, and revealed in its midportion a firm bluish mass 2 centimeters in diameter, which

was easily enucleated. No leakage of pancreatic secretion occurred. Following operation the blood sugar determinations ranged from 107 to 92 milligrams per 100 cubic centimeters and no further attacks occurred. The tumor was composed of B-cells of the island of Langerhans type.

CASE 7. (Barnes Hospital, St. Louis.) Adenoma of the islands of Langerhans with hypoglycæmia. Womack, Guagi, and Graham. J. Am. M. Ass., 1931, xcvii, 831.

A farmer, aged 44 years, one morning while doing chores before breakfast, noted a mental confusion comparable to intoxication which was completely relieved by eating breakfast. A second similar attack a week later was followed by increasingly severe seizures resulting finally in periods of unconsciousness, controlled completely by giving food. Various examinations were made and a tentative diagnosis of brain tumor suggested. The attacks then appeared before rising in the morning characterized by mental confusion, talking at random, and twitching movements, especially about the face. Symptoms apparently referable to the gall bladder developed, for which the gall bladder and appendix were removed, without relief. His wife then noted that repeated feedings during the night and the frequent ingestion of candy during the day prevented the attacks.

Physical examination was practically negative. The basal metabolic rate was + 3 per cent. After 9 hours of fasting, his blood sugar dropped to 50 milligrams per 100 cubic centimeters of blood. In this state his face was expressionless, pupils dilated, speech incoherent. One hundred and twenty grams of dextrose ingested by mouth restored him to a normal state. At the end of 7 hours he was again mentally confused. Epinephrin was administered and there was a temporary relief from the mental confusion with a definite rise in blood sugar. At operation, February 4, 1931, a small tumor, only 0.5 centimeter in diameter, was excised from the pancreas, and following the operation there were no further attacks. A 12 hour fast brought on no symptoms and his blood sugar did not fall below 90 milligrams per 100 cubic centimeters of blood. The tumor proved to be an adenoma of the islands of Langerhans.

CASE 8. (Mayo Clinic.) Hyperinsulinism. Report of two cases. Allan. Arch. Int. Med., 1929, xliv, 65.

A man, aged 47 years, was first seen in October, 1928, 4 years after the onset of weakness and stupor which was followed by convulsive seizures, disturbances of sleep, and somnambulism. He noticed that eating relieved the symptoms or checked the attacks so that he began to take food three times during the night as well as between meals. In spite of precautions, attacks of weakness and stupor occurred with increasing frequency, especially after exertion, and he was obliged to give up his work. About 2 months before admission, he was in a hospital, where food was not given after 5:30 p.m. Attacks occurred during the night, in which he became irrational and maniacal so that he was confined in a straight jacket on several occasions. Recovery occurred spontaneously after several hours.

Examination of the blood showed that the sugar content fell when food was not taken, sometimes reaching 0.04 per cent. Hypoglycæmic symptoms usually appeared when the blood sugar fell below 0.05 per cent. The ingestion of food with the equivalent of from 400 to 450 grams of dextrose prevented hypoglycæmic symptoms when given at suitable intervals. Epinephrin and solution of pituitary showed transitory effects in checking hypoglycæmia. Ephedrin also appeared to have some influence. At the operation, sometime after his first admission, the pancreas appeared to be normal. A portion weighing 8 grams was excised. Microscopical examination did not disclose distinct changes in the islands. The level of blood sugar fluctuated, and was not below normal until the fifth day, when the administration of dextrose was delayed until 11:30 a.m. The blood sugar fell to 0.066. From this time on, food was given three times during the day and three times during the night. It was apparent that the tendency to hypoglycæmia had returned. Convalescence was satisfactory, but it was necessary to continue the regular administration of food. The condition since has been about the same as it was before the operation.

CASE 9. (Pennsylvania Hospital, Philadelphia.) Adenoma of the islands of Langerhans with associated hypoglycæmia. McClenahan and Norris. Am. J. M. Sc., 1929, clxxvii, 93.

A colored male of 41 was admitted to the hospital on December 15, 1927, with the complaint of attacks of loss of memory preceded for several months by a very queer feeling, not accurately localized but apparently relieved by the ingestion of food. He was admitted in coma but within 1½ hours he had regained consciousness and was anxious to go home. A provisional diagnosis of epidemic encephalitis was made. Eleven hours after the usual hospital supper, he was again in coma which continued until his death 70 hours after admission.

Three successive blood sugar estimations at 24 hour intervals were 40 milligrams per 100 cubic centimeters, 42 milligrams, and 38 milligrams; in spite of the administration of glucose intravenously, by gavage, and by rectum. The autopsy revealed a tumor of the midportion of the pancreas, 15 by 7 by 16 millimeters in size, which had a delicate fibrous capsule, and the cells of which showed an alveolar arrangement, suggesting the adenomatous character of the lesion.

CASE 10. (Milwaukee County Hospital.) Carcinoma of the islands of the pancreas. Thalhimer and Murphy. J. Am. M. Ass., 1928, xci, 89.

A woman, aged 57 years, was admitted to the hospital in July, 1927, in a stuporous state, unable to answer questions, but not unconscious. About 2½ years before admission she began to have attacks characterized by somnolence, followed by great

restlessness and irritability. The attack would last about one day, and on the following day she usually slept most of the time. In the beginning the attacks came at regular intervals, varying from 2 weeks to 2 months. During the last year they came more frequently and averaged about three a week until 1 month prior to entering the hospital, when she began to have them every day. For the past year epileptiform convulsions accompanied these attacks, but she did not foam at the mouth or completely lose consciousness during the attack.

After entrance to the hospital, the patient remained in a semiconscious state most of the time. The seizures came regularly every forenoon about 9 o'clock. They were not severe and were not accompanied by stertorous breathing, unconsciousness, cyanosis, or foaming at the mouth. Usually the attack lasted from 30 minutes to 1 hour. Following this she slept for a few hours but could be aroused. Although she perspired mildly after the convulsions, it cannot be said that this was more than a minor symptom of the disease.

Blood sugar determinations on July 21 were 60.6 milligrams and on August 13, 33.5 milligrams per 100 cubic centimeters of blood. During the second week of August the convulsions came on about three times a day; following each attack the patient sank into a state of coma, and slept several hours. She died on August 18 after a prolonged state of coma.

At necropsy the pancreas showed a small tumor, 1.5 by 1 centimeters, located about 4 centimeters from the tail end, incompletely encapsulated and invading the surrounding pancreatic tissue. A diagnosis of carcinoma of the islands of Langerhans was made on the microscopic appearance.

It is apparent from the descriptions of the recorded cases that hyperinsulinism with its concomitant hypoglycæmia is a recognizable clinical syndrome, insidiously progressive in its course, characterized by symptoms of weakness verging on exhaustion, nervous irritability and anxiety, easy fatigability, extreme hunger, muscular twitchings and tremors, imperfect and hazy vision, diplopia, unsteadiness of gait, excessive perspiration, loss of emotional control, proceeding in the more serious cases to mental confusion, disorientation, epileptiform attacks, convulsive seizures, syncope, semistuporous states, coma, and finally death. These are the exact symptoms noted clinically due to an overdose of insulin and are directly commensurate with the resulting hypoglycæmia. Patients themselves frequently discover the beneficent effects of food in averting attacks.

Hypoglycæmia has been described in other conditions as well. Josephs and later Griffith described a series of cases of convulsions in infancy and childhood which they attributed to hypoglycæmia, the etiology of which they did not understand. In a case described by Griffith, a boy of 4 months suffered repeated convulsions which recurred at irregular intervals, until at the age of 2 years and 4 months, it was suggested that they resembled those found in hypoglycæmia. At this time during an attack in which he became unconscious, febrile, spastic, and vomited, an examination of the blood sugar showed only 20 milligrams per 100 cubic centimeters of blood. An intravenous injection of 100 cubic centimeters of a 10 per cent solution of dextrose resulted in prompt and complete recovery from this attack as also in four other similar seizures.

Cammidge and Wagner and Parnas have described cases of spontaneous hypoglycæmia which they thought were hepatic in origin, and Harris and later Jonas called attention to a remarkably lowered blood sugar in certain patients complaining of gastro-intestinal symptoms, weakness, and extreme fatigue. Subsequently Gougerot and Peyre and Sendrail and Planques made similar reports. Hyperinsulinism or dysinsulinism was advanced as the cause of these symptoms, but it remained for Wilder and his associates (Case 1) to present pathological proof of the association between spontaneous hypoglycæmia and hyperinsulinism.

It is possible that another explanation for hypoglycæmia lies in the experience recorded by Wadi, in which a typical case of Addison's disease with destruction of the entire suprarenal system was characterized by severe comatose attacks accompanied by a pronounced hypoglycæmia. These attacks were for a time aborted by administration of glucose.

Nielsen and Eggleston recently described 3 cases of epileptiform seizures accompanied by a lowered blood sugar and an altered blood pressure in which great improvement was obtained by frequent feedings and the administration of dessicated whole suprarenal gland by mouth. Frequent feedings alone did not work as well as when combined with the suprarenal gland. They postulated a dysinsulinism or hyposuprarenalism as the probable causative factors.

Several years ago a condition of hypoglycæmia was demonstrated 18 hours following subtotal thyroidectomy for Graves' disease (5, 8). An antagonism between thyroxin and insulin has been hinted at by various writers, and it is suggested that the removal of a hyperactive thyroid gland results in a temporary overaction of its antagonist, the pancreas. However, the interrelationship of the thyroid, adrenal, pituitary, and pancreatic glands is so intimate and the mechanism of their interactions with reference to sugar metabolism so obscure, that one can do little but theorize, and that not very intelligently. For the moment one can simply present the facts in the hope that they can be pieced together subsequently.

In the three instances in which small adenomata were removed at operation with complete recovery, one is surprised to find how small these tumors actually were. In the two cases from the Barnes Hospital, Cases 6 and 7, the first tumor measured 2 centimeters in diameter, and the second only 0.5 centimeter in diameter. The case from the Toronto General Hospital yielded a carcinomatous tumor only 1.5 centimeters in diameter. Two other instances in which proved hypoglycæmia existed before death, Cases 9 and 10, yielded tumors only 1.5 centimeters in diameter. Shields Warren records 4 instances of so called adenomata of the islands of Langerhans found incidentally at necropsy measuring 1.7 millimeters, 1.3 millimeters, 1.2 millimeters, and 9 millimeters in diameter, respectively. These patients all died of other causes and gave no recognizable clinical evidence of hypoglycæmia.

It is highly probable that in the 4 patients operated upon by resection of portions of the pancreas without conspicuous improvement in symptoms (Cases 2, 3, 4, 8) small adenomata in the remaining pancreas may well have been overlooked. When operation is done for hypoglycæmia careful palpation and inspection of the body and tail of the pancreas is indicated to detect the comparatively small tumors that could account for the clinical symptoms. If such a search is fruitless, it would appear necessary to mobilize the pancreas fairly completely and to remove at least four-fifths of the gland. Mobilization of the pancreas could be facilitated markedly by removing the spleen with it, thus obviating the necessity of ligating the innumerable tributaries of the splenic artery and vein which course along the upper border of the pancreas.

SUMMARY

Hyperinsulinism with its resulting hypoglycæmia produces symptoms of weakness verging on exhaustion, mental confusion, disorientation, epileptiform attacks, convulsive seizures, syncope, unconsciousness, coma, and death. Clinically and anatomically it has been demonstrated in connection with carcinoma of the islands of Langerhans, adenoma of the islands of Langerhans, and hyperplasia of the pancreas. The last condition is still purely hypothetical and it may ultimately be found that the hypoglycæmia in similar cases is dependent not upon simple hyperplasia of the gland but upon small adenomata embedded in the gland and therefore not easily demonstrable at operation. The presence of such small adenomata should, however, be carefully sought for in any case operated upon for spontaneous hypoglycæmia before resorting to partial pancreatectomy. Case 3 is presented as the second instance of spontaneous hypoglycæmia due presumably to simple hyperplasia of the pancreas, improved by partial resection of the pancreas.

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THE INFLUENCE OF ENDOMETRIUM UPON THE RABBIT OVARY AFTER HYSTERECTOMY

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IT is a generally accepted clinical observation that hysterectomy, even with the conservation of one or both ovaries, hastens the onset of symptoms of the menopause. A second clinical observation is that these symptoms are less likely to develop if the amputation is performed high enough to insure the retention of sufficient endometrium to permit at least a scanty menstruation. These two observations have led to the theory that the endometrium produces a hormone essential to the normal functioning of the ovary; its removal disturbs the normal endocrine activity of the latter organ which dysfunction in turn is responsible for the early onset of the menopause. In the present experimental investigation, an attempt has been made to find out whether the endometrium is essential to the normal functioning of the ovary.

Dysfunction of the ovary following hysterectomy can be studied indirectly from the anatomical point of view. Little knowledge is available regarding the structure of the *human* ovary, permitted to remain *in situ* for a considerable period of time following operation. Though such ovaries have been examined, none has been studied in serial section; consequently, until an adequate number of these studies are made, the histological picture of the ovary after hysterectomy will be understood best by a study of serial sections of the animal ovary.

The present experimental investigation concerns the gross and microscopical structure of the rabbit ovary removed some months following hysterectomy, and is based upon observations on 52 animals. Endometrium was autotransplanted in half of these at the time hysterectomy was performed.

The object of the study was to determine: First, if structural changes occur in the ovary of the rabbit as a result of hysterectomy; second, if so, their nature; and third, whether loss of endometrium is a factor in bringing about these changes.

REVIEW OF LITERATURE

Human ovary after hysterectomy. Twenty-two reports were studied, which dealt with the condition of human ovaries removed some weeks, months, or years following hysterectomy (1–5, 7–14, 17, 21, 23–26, 31, 32, 35). Among the gross pathological changes, cysts were noted by ten observers and atrophy by five. These were the only gross findings common to any two reports. Eight of the 22 authors reported microscopic findings. Five of the 8 observed nothing abnormal (3, 8, 9, 11, 17); of the other 3, Hawks and Vineberg observed cystic changes, and Werth reported the presence of large follicles and the absence of ova.

These statistics are probably misleading, with respect to the frequency with which abnormal developments occur in conserved ovaries, as obviously few ovaries which are normal, and hence produce no trouble, are removed at a second operation.

Animal ovary after hysterectomy. Of 19 studies dealing with the anatomy of the animal ovary, 17 included microscopic examina-

tion. In 6 of the 17 studies, the ovaries were described as being microscopically normal; in the remaining 11, alterations were observed. Schubert saw no ova, Lindig observed dilated follicles; Terada found follicular atresia; Keitler and Jacobsohn noted a smaller number of follicles than normally, while Loeb and Takakusu both described large corpora lutea, which were believed to have resulted from an inhibition of the regressive power of these bodies. Degenerative changes were observed in four experiments (18, 22, 33, 34) but in only two were cysts found (19, 27).

Human ovary after hysterectomy and uterine transplantation. Three reports concerned the transplantation of human uteri, or portions of endometrium at the time of hysterectomy, but gave no later description of the ovaries (28, 33, 34).

Animal ovary after hysterectomy and uterine transplantation. Four previous workers reported the results of their efforts to influence ovarian function experimentally by means of uterine transplantation. Schubert transplanted the whole uterus of a goat, with no resulting effect upon the estrous cycle. Zimmermann (33, 34) transplanted pieces of endometrium into the abdominal wall in hysterectomized rabbits, and found that regressive changes in the retained ovary were inhibited as long as sufficient uterine tissue remained viable. Takakusu transplanted portions of uterus into the abdominal wall of one series of rats at the time of hysterectomy, and of a second series of these animals 3 or 4 weeks after hysterectomy. The ovaries of the group submitted to an immediate transplant were found subsequently to be more nearly normal in microscopical appearance, than those from the group submitted to transplantation 3 to 4 weeks after their hysterectomy was performed. Parfenoff, using a single series of mice, found that hysterectomy without endometrial transplantation produced follicular atrophy. With the use of endometrial transplants into the abdominal wall, he was able to stimulate the growth of new follicles and fresh corpora lutea.

EXPERIMENTS

Materials and methods. Sixty-four adult rabbits (8 pregnant, 26 exhibiting varying degrees of heat, and 30 not in heat), were subjected to hysterectomy, half of the group receiving, simultaneously, autotransplants of endometrium in the abdominal wall. The operations were conducted under either ether inhalation anæsthesia, or following the intraperitoneal injection of a watery solution of "amytal" (iso-amyl-ethyl-barbituric acid). In each instance, the entire uterus was removed, including the upper half of the vagina and the portion of each oviduct next to the uterus. Three pieces of endometrium, approximately 3 to 4 millimeters in largest diameter, were then placed in a pocket in each rectus abdominis muscle. During the operation, touching of the ovaries or traction on the mesovarium was avoided. The animals were isolated during the period of wound healing, after which they were herded together until sacrificed.

During the interval between operation and sacrifice, no attempt was made to test ovarian function by the willingness of the female to accept the male. Since the rabbit ovulates only at the time of copulation or of other sexual excitement, as when one female in heat covers another, had copulation been permitted and had it occurred in some cases only, it would have injected a variation into the follicular picture presented by the entire group.

Of the original 64 animals operated upon, 52, divided equally between the transplant and the non-transplant groups, lived 6 months. All were killed by chloroform inhalation, 39 at the end of 6 months, and 3 months later, or 9 months following hysterectomy, the 13 remaining were sacrificed. The gross appearance of the ovaries and transplants was recorded and both were prepared for sectioning, Susa fixation being used. For control purposes, ovaries were removed from 13 non-hysterectomized adult rabbits, which were definitely not in heat.

RESULTS

Classification of ovaries. The ovaries fell readily into 3 treatment groups: Group I, ovaries from control animals (non-treatment group). Group II, ovaries from animals subjected to a simultaneous hysterectomy and autotransplantation of endometrium (trans-

TABLE I.—NUMBER OF SECONDARY FOLLICLES

Group	Serial number	Weights		Secondary follicles
		Rabbit kgms.	Ovary mgms.	Number
I Control	C	2.6	90	88
	J	2.8	95	129
	L	2.7	70	50
	O	2.9	100	151
	Q	3.5	100	77
	Average	2.9	91	99
II Transplant	B 7	4.2	110	72
	B 9	4.0	85	29
	B 10	4.0	130	74
	B 12	3.5	110	64
	B 14	3.1	120	110
	Average	3.76	110	69.8
III Non-transplant	A 6	3.4	90	34
	A 7	3.9	80	59
	A 8	3.4	80	59
	A 9	4.3	85	44
	A 10	3.5	100	60
	Average	3.7	87	51.2

Showing (a) the number of secondary follicles by actual count, 0.25 millimeter or more in diameter, observed in (I) 5 control ovaries, (II) 5 ovaries from animals subjected 6 months previously to a simultaneous hysterectomy and autotransplantation of endometrium, and (III) 5 ovaries from animals subjected to hysterectomy without transplantation of endometrium, together with (b) the weights of the animals and (c) the weights of the ovaries which contained the counted follicles. Note that, on the average, the operated upon animals (Groups II and III) possessed fewer secondary follicles than the control animals (Group I), and that the animals subjected to a transplantation of endometrium (Group II) possessed a larger number of secondary follicles than the ones subjected to the hysterectomy without the transplantation of endometrium (Group III). Also observe that the average weights of the ovaries in the different groups did not vary proportionally with the numbers of follicles in the same groups.

plant group). Group III, ovaries from rabbits subjected to a hysterectomy without an autotransplantation of endometrium (non-transplant group).

Gross appearance of ovaries. The ovaries of the 52 animals operated upon (Groups II and III) were in the resting state. Whether this uniform condition was a sequel of the hysterectomy or due to other circumstances, cannot be stated.

The ovaries of 49 of the 52 rabbits were grossly normal. The remaining animals exhibited one normal and one abnormal ovary apiece. In each case, the latter ovary formed part of a mass composed chiefly of oviduct distended with clear fluid, apparently due to blocking of the uterine end by a ligature. In these three instances, the ovaries were thinned out and their outlines were very indefinite. In no case did the ovaries of the animals operated upon, exhibit grossly either signs of atrophy or of cyst formation other than that mentioned above.

Twenty-six ovaries from the non-treatment group (I), 50 from the transplant group (II), and 51 from the non-transplant group (III) were weighed and measured. There were no significant differences in the size or weight of any of these ovaries.

Gross appearance of transplants. Each of the 26 animals which received autotransplants of endometrium, when killed possessed at least one piece of engrafted tissue of considerable size. In 20 cases, bilateral transplants were present, in the remaining 6 only a single one. The transplants were multilocular cysts, the largest of which reached a diameter of 25 millimeters. In animals killed 6 months after operation, the transplants were slightly larger on the average than those in animals killed 9 months after operation.

After they had remained in fixative for some time, the transplants were bisected. The majority contained clear fluid, others possessed a yellow or white granular material, and in one or two, a gelatinous substance was present. One transplant from each of 20 of the animals was studied microscopically; half of each one was cut serially in sections 6 micra thick and each fiftieth section was examined. These transplants were removed from the 20 animals whose ovaries were studied microscopically.

Microscopical appearance of transplants. In 18 of the 20 transplants (Fig. 1), the cells lining the cysts varied in shape; some were ciliated, though the majority were not. Most of them were normal in appearance, only a few exhibited degeneration, which was extensive in only 2 cases. The degenerated cells desquamated and were found suspended in the liquor which filled the cyst cavities. In 2 cases, the cells lining the cysts dipped into

the underlying tissue, forming structures similar to the small uterine glands (Fig. 2).

The tunica propria, which was composed of a loose sheet of typical fibroblasts, varied greatly in thickness. It was rich in blood vessels and poor in lymphocytes and leucocytes. Bundles of involuntary muscle fibers were characteristic of most of the transplants, in some cases forming a dense sheath.

Two of the 20 transplants were in the process of degeneration; in them the cyst cavity was narrow. The epithelial lining was almost absent, and the tunica propria also showed signs of degeneration. This was associated with hæmorrhage and an invasion of leucocytes and lymphocytes.

Microscopic appearance of ovaries. Microscopic study of the ovaries included: (1) a count of the secondary follicles (those above 0.25 millimeter in diameter and with cavity formation); (2) measurement of the largest diameter of each; (3) an estimation of the number of primary follicles; (4) the frequency with which atresia occurred; and (5) the condition of the remaining tissues in the organ.

One ovary, selected at random, from each of 19 non-transplant, 20 transplant, and 7 control animals, was cut parallel to its long axis, in serial sections 6 micra thick, which were stained with hæmatoxylin-eosin.

Number of secondary follicles. The secondary follicles in 15 ovaries, which included 5 from control animals, and 5 each from the transplant and the non-transplant groups, were counted in the following manner: Each sixth section, in its entirety, was projected on paper at a magnification of 20 diameters, outlined in pencil, and each secondary follicle, with an outside diameter of 5 millimeters or more when projected, was also outlined. This minimum follicle size was selected arbitrarily in view of the difficulty of measuring accurately projected follicles of a lesser diameter. The first section of each follicle to appear was given an identification number, which it retained as its subsequent sections reappeared on other slides.

The number of these secondary follicles in the 15 ovaries, together with the weights of the animals, and of the ovaries which contained the counted follicles, are recorded in Table I. The ovaries of the animals subjected to a simple hysterectomy (Table I, Group III), exhibited approximately half the number of follicles possessed by the control series (Table I, Group I), though the weights of the ovaries in these two groups were approximately the same. The ovaries of the transplant group (Table I, Group II) possessed a follicular count midway between those of the controls (Group I) and of the non-transplant animals (Group III). Significant differences seemed to exist between the actual number of secondary follicles in these three groups of ovaries as shown numerically in Table I and graphically in Figure 3.

The relative number of secondary follicles in the three treatment groups was arrived at in another manner: The number of sections of secondary follicles present in each sixtieth section of each of the 15 ovaries was counted. The total of these sections in all of the sixtieth sections of each ovary gave a relative figure, but not an absolute one, for the number of follicles present. The average of these estimations for the 3 treatment groups of ovaries

TABLE II.—NUMBER OF SECONDARY FOLLICLES IN RABBIT OVARY AFTER HYSTERECTOMY

Treatment group	Group A			Group B	
		Follicles			Follicles
	No. of animals	Actual count	Average estimated ratio	No. of animals	Average estimated ratio
I Control	5	99.0	83.8	2	113.5
II Transplant	5	69.8	66.8	13	50.0
III Non-transplant	5	51.2	42.8	16	37.0

Showing the results of 2 methods for establishing the ratios between the number of secondary follicles (those with cavity formation) in one ovary from each of (I) 5 control animals, (II) 5 subjected to simultaneous hysterectomy and autotransplantation of endometrium, and (III) 5 subjected to hysterectomy without transplantation of endometrium. The average number of secondary follicles (.25 millimeter or more in diameter) *by actual count* is recorded for the 5 ovaries (Group A) in each of the three treatment groups and the average of the total number of sections of all follicles seen in each sixtieth section of each of the same ovaries is also shown (Group A). Contrasted with these, are the averages of the total number of sections of all follicles seen in each sixtieth section of 31 additional ovaries (Group B). Note that the averages of the estimated ratios between the numbers of sections of secondary follicles in Groups A and B in the three treatment groups are relatively consistent with the averages of the actual counts of the follicles in Group A.

TABLE III.—NUMBER OF NORMAL PRIMARY FOLLICLES AND ATRETIC PRIMARY AND SECONDARY FOLLICLES

Condition of follicles	Ovaries showing *many* follicles		
	7 control Per cent	19 non-transplant Per cent	20 transplant Per cent
Normal	100	63	60
Atretic	100	183	174

Showing the estimated relative number of (a) normal primary follicles and (b) atretic primary and secondary follicles in one ovary from each of (1) 7 control animals, (2) 19 animals subjected to a hysterectomy 6 months previously, and (3) 20 animals subjected to a simultaneous hysterectomy and autotransplantation of endometrium, also 6 months previously. The number of normal and atretic follicles is expressed as the percentages of the number of ovaries which possessed many as compared with few of these follicles, on the basis that 100 per cent of the control ovaries possessed many normal primary follicles, and many atretic primary and secondary follicles. Note the decreased percentages of ovaries of the two groups operated upon which possessed many normal primary follicles and the *increased* percentages of ovaries in both groups operated upon, which exhibited many atretic follicles. In other words, the animals operated upon possessed fewer normal primary follicles and more atretic primary and secondary follicles than did the ovaries of the control animals.

is recorded in Table II. The ratio between these estimated averages (Table II, Group A) was found to be consistent with the ratios observed between the actual counts of the follicles in the same ovaries (Table II, Group A). Since this shorter method of estimating the relative number of follicles in the 3 treatment groups gave results which were consistent with those secured by actual count, it was used in determining the relative number of follicles in the ovaries of 31 additional rabbits (Table II, Group B). The constant relation between the actual count of the follicles in Group A, and the estimations of their numbers in Groups A and B, emphasizes the constancy of the differences in the numbers of follicles in the control, transplant, and non-transplant groups.

Size of secondary follicles. The size of each secondary follicle in the 15 ovaries (Table I, and Table II, Group A) was recorded in terms of its maximum diameter. It was found that the follicles in the ovaries of both groups of animals operated upon reached the same ultimate size as did those in the control group. From this observation, it is concluded that growth of the measured secondary follicles, in the ovaries of animals operated upon, was not interfered with by removal of their uteri. This fact is of interest in view of the small number of follicles found after hysterectomy.

Number of primary follicles. The number of primary follicles was not counted but only estimated. The ovaries of the control animals possessed either a continuous layer of primary follicles in the cortex, or occasional interruptions in this layer of follicles, which were also noted in the ovaries of some of the animals operated upon. Such ovaries were described as possessing many primary follicles. In case larger gaps existed in the layer of primary follicles in the ovaries of animals operated upon, or if the follicles appeared only in scattered groups, these ovaries were described as possessing few follicles.

Comparing the percentages of ovaries in the three treatment groups, which presented many in contrast to few normal primary follicles (Table III), it becomes evident that in the 2 groups operated upon (II and III), there were fewer ovaries containing many primary follicles. In other words, the ovaries of the animals operated upon (Groups II and III) possessed fewer primary follicles than did those of the control animals (Group I). The question whether this marked difference was due (1) to failure of the primary follicles to form, or (2) to the early degeneration of a large number of them will be discussed later.

Atresia. The ovaries of control and operated upon animals possessed varying numbers of atretic primary and secondary follicles. These were not counted but only estimated. Where they were more numerous, the term many atretic follicles was used, where less frequent, the term few. The number of ovaries (expressed in percentages) of animals operated upon which exhibited many atretic primary and secondary follicles is recorded in Table III, on the basis that 100 per cent of the control ovaries possessed many of these follicles. It will be noted that atresia was observed more frequently in the ovaries of the animals operated upon than in the controls, and also that transplantation of endometrium appeared to lessen the amount of atresia.

TABLE IV.—AMOUNT OF STROMA

Stroma	Ovaries		
	7 control Per cent	19 non-transplant Per cent	20 transplant Per cent
Well developed	100	58	75

Showing the frequency with which well developed stroma was observed in one ovary from each of (1) 7 control rabbits, (2) 19 subjected to a hysterectomy 6 months previously, and (3) 20 animals subjected to a simultaneous hysterectomy and autotransplantation of endometrium also 6 months before. The amount of stroma is expressed as the percentage of ovaries which possessed a well developed stroma, as compared with those which had a poorly developed stroma; on the basis that 100 per cent of the control ovaries possessed a well developed stroma. It will be noted that more of the ovaries of the 20 animals subjected to a simultaneous hysterectomy and autotransplantation of endometrium exhibited well developed stroma than did the ovaries of the 19 animals subjected to hysterectomy without autotransplantation of endometrium.

TABLE V.—AMOUNT OF INTERSTITIAL TISSUE

Amount of interstitial tissue	Ovaries		
	7 control Per cent	19 non-transplant Per cent	20 transplant Per cent
Much	100	107	90

Showing the estimated amount of interstitial tissue in one ovary from each of (1) 7 control animals, (2) 19 animals subjected to a hysterectomy 6 months previously, and (3) 20 animals subjected to a simultaneous hysterectomy and an autotransplantation of endometrium also 6 months previously.

The amount of interstitial tissue is expressed as the percentage of ovaries which possessed much tissue in contrast to the percentage which possessed a moderate amount, on the basis that 100 per cent of the control ovaries possessed much interstitial tissue. Note that the ovaries of the 2 groups of operated upon animals possessed approximately the same amount of interstitial tissue as those of the control animals.

Germinal epithelium. The histological picture of the germinal epithelium of the groups operated upon was identical with that of the controls.

Stroma. In the ovaries of the control animals, the amount of stroma, its distribution and structure, with one exception, were found to be uniform (well developed). The larger blood vessels were surrounded with abundant connective tissue, which followed the smaller ones into the cortex, and distinct septa of connective tissue were present between the different sized groups of interstitial cells.

In the exception just mentioned, the connective tissue formed a sheath of only medium thickness around the larger vessels, and the septa between the groups of interstitial cells were also more delicate. The term "moderately developed" stroma was applied to this case. This type of stroma was observed in quite a large number of the ovaries of the animals operated upon. In the cases in which the connective tissue septa in some ovaries were almost entirely absent, and the vessels were surrounded with only a thin layer of connective tissue, the stroma was termed poorly developed.

The number of ovaries (expressed in percentages) in the different groups, which possessed a well developed stroma is shown in Table IV. These figures are based on the finding that 100 per cent of the control ovaries possessed a well developed stroma. It is evident (1) that more control animals exhibited a well developed stroma than did the animals operated upon and (2) that the stroma was better developed in the ovaries of the transplant group than in those of the non-transplant group.

Interstitial tissue. The amount of interstitial tissue was found to be approximately the same in the ovaries of control animals and animals operated upon (Table V). The interstitial cells, however, varied in size, shape, and structure. Four types connected with transitional forms were observed (Table VI).

Type I. This cell, small, polygonal in shape, its nucleus about the size of a red corpuscle, was surrounded with a narrow layer of cytoplasm, which was usually shrunken. If properly preserved and stained, it was slightly granular and neutral in its reaction to the stains.

Type II. The nucleus of this type of cell was polygonal and slightly larger than that of Type I; its cytoplasm was abundant and contained granules which showed a strong affinity for the acid dye. It contained vacuoles of varying sizes, the largest sometimes the size of its nucleus.

Type III. The cells of this type resembled those of Type II. However, the individual cell and its vacuoles were considerably larger than those of Type II.

TABLE VI.—TYPES OF INTERSTITIAL CELLS

Cells	Ovaries		
	7 control Per cent	19 non-transplant Per cent	20 transplant Per cent
Type I Prevalent, or equal to Type II	100	42	65
Type II Prevalent, or equal to Type I	100	68	42
Type III Many	71	42	16
Absent	29	10	0
Type IV Many	0	42	32
Absent	43	10	5

Showing the frequency with which four types of interstitial cells were observed in one ovary from each of (1) 7 control rabbits, (2) 19 animals subjected to a hysterectomy 6 months previously, and (3) 20 animals which at the same time were subjected to a simultaneous hysterectomy and autotransplantation of endometrium. The number of cells of each type is expressed as the percentage of ovaries which possessed the type of cells recorded in the left column, on the basis that 100 per cent of the control ovaries possessed approximately equal numbers of cells of Types I and II. Note that both groups of animals operated upon possessed fewer of the cells of Types I and II, and that the cells of Type I were seen more frequently in the ovaries of the transplant group than in those of the non-transplant group.

Type IV. These cells looked like fat cells. They were large, round, and contained a few large vacuoles or perhaps only one, and some remnants of granular cytoplasm.

In spite of these dissimilarities, these four types of cells appear to be true interstitial cells. Their differences might be explained on one of two assumptions: Either they represent cells which are functioning differently, or they are steps in a slow but progressive form of degeneration.

DEDUCTIONS FROM EXPERIMENTS

Although scattered data have appeared in the literature concerning the influence of hysterectomy (upon both humans and animals), in producing cysts in ovaries which have been left *in situ* following this operation, our large number of experiments gave no evidence that this is so in the case of the rabbit. From our observations, we conclude that loss of endometrium plays no rôle in the production of ovarian cysts in the rabbit.

Endometrial autotransplants appear to grow readily for a short time in the abdominal wall of the rabbit. Ultimately, however, they lose their typical structure, and become cystic. In view of the several histological differences between the ovaries of the animals which received transplants and those which did not, it would appear that the transplants functioned for a while at least. In this connection, it must be remembered that transplanted endometrium, even if entirely healthy, is less in amount than in the normal animal. Consequently, if inhibiting or degenerative changes in ovaries result from removal of all endometrium, these same changes, to a lesser extent, might be expected in all transplant cases, especially in those in which the transplant failed to grow or later atrophied.

It is also quite likely that the endometrium left after high amputation of the human uterus is less subject to degenerative changes than that transplanted into the rectus muscle of the rabbit. Obviously then, the ovaries remaining in the human being which retained high cervical endometrium would be less likely to exhibit inhibiting or degenerative changes than would those in animals whose only endometrial tissue was in the rectus muscle.

The decreased number of primary and secondary follicles observed in the two groups of operated upon animals raises the question of the manner in which these decreases were brought about. It is possible that the reduction in the number was due to (1) an inhibition of formation of new follicles, or (2) a degeneration of existing follicles, or (3) a combination of the two. The small number of primary follicles in the cortex of the ovaries of the animals operated upon suggests that fewer of them formed than normally, while the increased number of atretic primary and early secondary follicles indicates that many follicles failed to develop normally. Atresia of primary and of small secondary follicles was more frequent than in the case of the larger secondary follicles. In view of these observations, and because the larger follicles of control animals and those operated upon all reached the same ultimate size, it would seem that the hysterectomy influenced chiefly the primary and the smaller secondary follicles, and that it acted mainly by inhibiting the formation of new

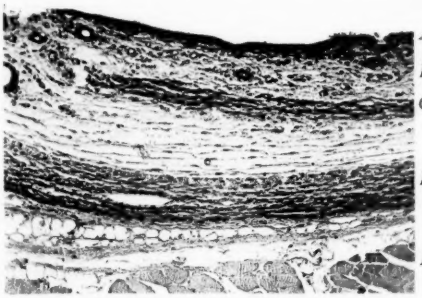

Fig. 1. Showing wall of typical endometrial cyst resulting from autotransplantation of endometrium into rectus abdominis muscle of rabbit when hysterectomy was performed 6 months previously. *A*, Epithelial lining of cyst; *B*, tunica propria containing several gland-like structures; *C*, smooth muscle fibers, probably uterine in origin; *D*, cyst capsule; *E*, rectus abdominis muscle. ×75.

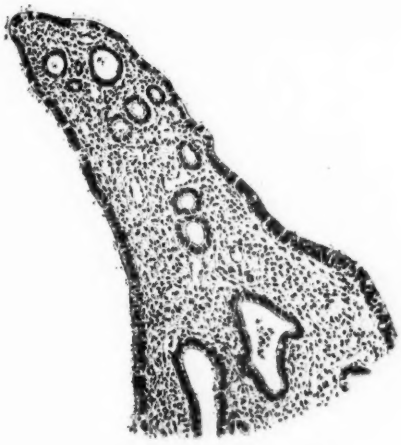

Fig. 2. Showing an endometrium-like structure which projected into the cavity of a cyst, resulting from the autotransplantation of endometrium into the rectus abdominis muscle of a rabbit when hysterectomy was performed 6 months previously. Note the ciliated epithelium on the surface and beneath it the numerous endometrium-like glandular structures.

follicles, since the absence of primary follicles in the cortex was more evident in most of the ovaries than was the presence of an undue amount of atresia.

The germinal epithelium presented nothing unusual from the anatomical point of view. The significant decrease in the estimated number of primary follicles in the ovaries of the animals operated upon and the actual decrease (40 per cent) in the number of counted secondary follicles, however, suggests that the operation must have influenced this tissue functionally, even if there was no observable anatomical alteration.

No evidence from the experience of others has been found which indicates that the stroma of the ovary is influenced by the action of any hormone, or that the connective tissue of any other organ is similarly affected (6). On the contrary, our findings point to (1) a definite difference in the amounts of stroma in operated upon and control animals, and (2) a difference in the amount of stroma in the transplant group as compared with the non-transplant group. From these observations, it might be concluded that the stroma is influenced by loss of the uterus and, therefore, that it is affected by hormones.

The interstitial tissue appeared to be constant in amount in the ovaries of both the operated upon and the control animals. Its amount, therefore, does not seem to have any direct or appreciable relation to loss of endometrium.

In the control ovaries, the more normal types of cells (I and II) predominated (Table VI), and, though those of Type III were seen, the cells of Type IV were absent. In the ovaries of the non-transplant group, the Type II cells were observed more frequently than in the transplant group. This indicates a shifting from the normal type of cell, following hysterectomy, to that of the cell which was either functionally different or degenerating, according to the interpretation of the change. Since the cells of Type I were found more frequently in the transplant group than in the non-transplant group, the conclusion may be drawn that the presence of the transplant tended to check the shifting process from Type I toward IV. The reason for this difference cannot be stated, though it might be assumed that the presence of the endometrium was a factor.

The arrangement of the cells of Type III in clusters of various sizes, suggests that these cells might have been mistaken by other observers for degenerating corpora lutea. How-

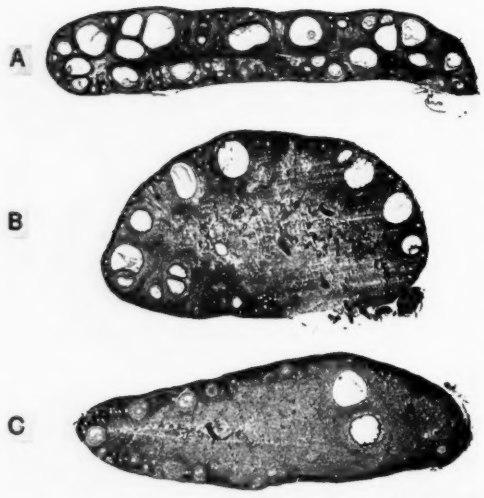

Fig. 3. Showing the relative number of secondary follicles (those with cavity formation) seen in A, the ovary of an adult rabbit in the resting stage; B, an ovary removed 6 months after a simultaneous hysterectomy and autotransplantation of endometrium; and C, an ovary removed after a hysterectomy, without transplantation of endometrium. Note that the ovary from the animal subjected to a hysterectomy and an autotransplantation of endometrium, B, possessed more secondary follicles than the ovary from the animal subjected to a hysterectomy without transplantation of endometrium, C, and that both of these ovaries possessed fewer secondary follicles than the control ovary, A.

ever, a careful search of all our material failed to disclose any remnant of a single corpus luteum.

The operation of hysterectomy appeared to have a definite influence upon the ability of the rabbit to exhibit heat. More than half of the hysterectomized animals, at the time of operation were either pregnant (8) or exhibited moderate degrees of uterine turgescence (26). Following the period of wound healing, the entire group was herded together. Yet in spite of this opportunity which was offered for the covering of one female by another, no remnants of corpora lutea were observed in any ovary to indicate that a pseudo-pregnancy had occurred, and therefore that estrus existed.

SUMMARY

1. Observations are recorded upon (a) the gross and microscopical appearance of the ovaries of 26 rabbits which were subjected to a hysterectomy 6 months or more previously, and upon (b) 26 which were subjected to a simultaneous hysterectomy and autotransplantation of endometrium.

2. The ovaries of both groups of hysterectomized animals exhibited grossly no significant differences from the ovaries of control (unoperated upon) animals, except that none of them showed any signs of follicular activity characteristic of estrus.

3. Microscopically, the ovaries of the hysterectomized animals differed from those of control (unoperated upon) animals by possessing: (a) fewer primary and secondary follicles; (b) more atretic follicles, chiefly primary; (c) less stroma; (d) more atypical interstitial cells.

4. In comparison with the ovaries of the animals subjected solely to a hysterectomy, the ovaries of animals subjected to a simultaneous hysterectomy and autotransplantation of endometrium microscopically exhibited: (a) more secondary follicles, (b) fewer atretic follicles, (c) more stroma, (d) a healthier type of interstitial tissue.

CONCLUSIONS

1. Hysterectomy upon the rabbit (a) inhibits the development of estrus, and (b) brings about changes in the microscopic structure of the remaining ovaries, which tend to be both inhibitory and degenerative in nature.

2. Autotransplantation of endometrium has a tendency to limit the extent of the inhibitory and degenerative changes which result from hysterectomy.

3. Evidence is brought forward to support the theory that the endometrium elaborates a hormone which influences the ovary.

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THE RELATION OF PULMONARY TUBERCULOSIS TO ANORECTAL FISTULÆ

A Clinical, Pathological and Bacteriological Study

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IN clinical interpretation it is common experience that views change as more accurate and detailed scientific observations serve as a basis for a clearer insight into the actual conditions present. Medical history is replete with interpretations and discussions on anorectal fistulæ, and the literature on this subject alone has assumed voluminous proportions. Several decades ago discussion centered about the question whether all anorectal fistulæ were of tuberculous origin or not, and proponents of either view were easily found. With the introduction of better scientific methods, agreement was more common and discussion was relegated mainly to an explanation of the origin of the condition, which probably will never entirely be settled and which so far as practice is concerned is of little actual importance. In the discussions of anorectal fistulæ over the decades, there is to be noted also the influence of changed conceptions regarding tuberculosis in general, and in this appears the controversy of aerogenic versus intestinal infection, and local versus hæmatogenous and lymphatic infection. Thus, historically Lockhart-Mummery, in 1929, advises us: "The operation for 'fistula-ano' is associated with the very earliest records of surgical literature" . . . "In the days of early civilization when cleanliness was a matter of secondary consideration—water being used chiefly for drinking purposes—and the horse was the only means of transport, fistula must have been even a more serious inconvenience than it is now." In looking up the records of St. Mark's Hospital, he found that since the year 1909 the number of cases of fistula has steadily diminished. The number in 1926 being a little over one-half the number admitted in 1909—a fact which is easily understood in the light of increasing sanitary hygiene. Regarding the primary cause he cites abscess in the tissues surrounding the rectum and classifies the causes as follows: (1) congenital cysts; (2) foreign bodies; (3) fissures or ulcers; (4) suppuration of the intramuscular glands, and (5) tubercle. Regarding the bacteriology he states: "Apart from tubercle, the nature of the infective organisms is probably not important. The pus from most fistulæ on culture shows a very mixed infection." Regarding the diagnosis of tuberculous fistulæ he states: "Such fistulæ (tuberculous) can generally be diagnosed from the appearance of the parts, but this is not entirely reliable. Examination of the pus or discharges for tubercle, is quite useless. Histological examination of a few pieces of the wall of the fistula is fairly reliable, but the only certain method is by inoculation into guinea pigs after concentration with antiformin."

Reviewing the current German views on the etiology of rectal fistulæ, Thoss, in 1920, cites Richard Volkmann and Franz Koenig as believing rectal fistulæ to be of tuberculous origin in the majority of cases, while De Quervain considers at least half of them to be tuberculous, and Melchior in 1910 cites an incidence of 61 per cent, and Goez reports 45 per cent in Munich. Opposing these views are those of Lanz who considers tuberculosis of little significance, those of Frey (1914) who found only 6.9 per cent to be tuberculous by macroscopic and microscopic examination of 72 patients operated upon. Frey insists that only the findings at the fistulous site are significant and the presence of tuberculosis elsewhere is not conclusive, while Melchior contends that even a negative microscopic examination cannot exclude the presence of tuberculosis in the fistulæ. The futility of arriving at conclusions from the methods used at that time is noted from this article.

In 1925 Fansler read one of his first contributions on the relationship of tuberculosis

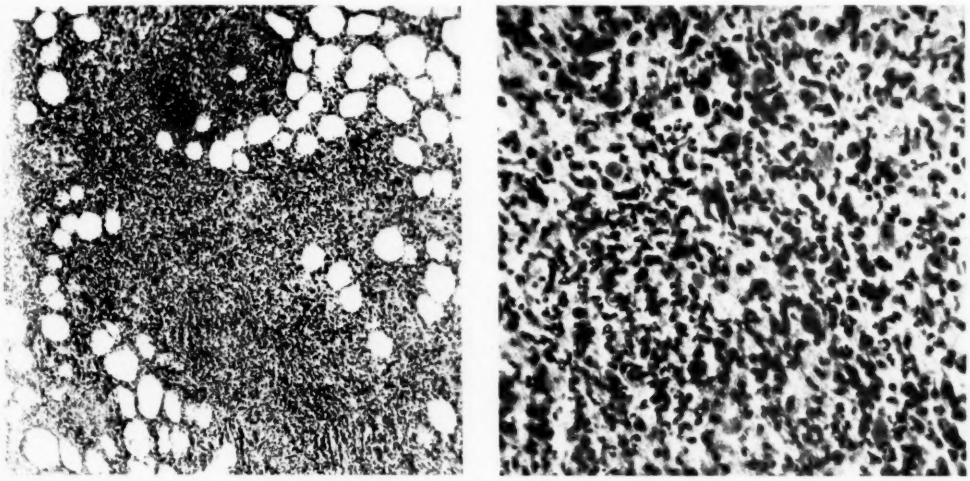

Fig. 1. Typical acute inflammatory (granulocytic) reaction in specimen from Case 157 found negative for tubercle bacilli by bacteriological examination. Left, low power; right, high power.

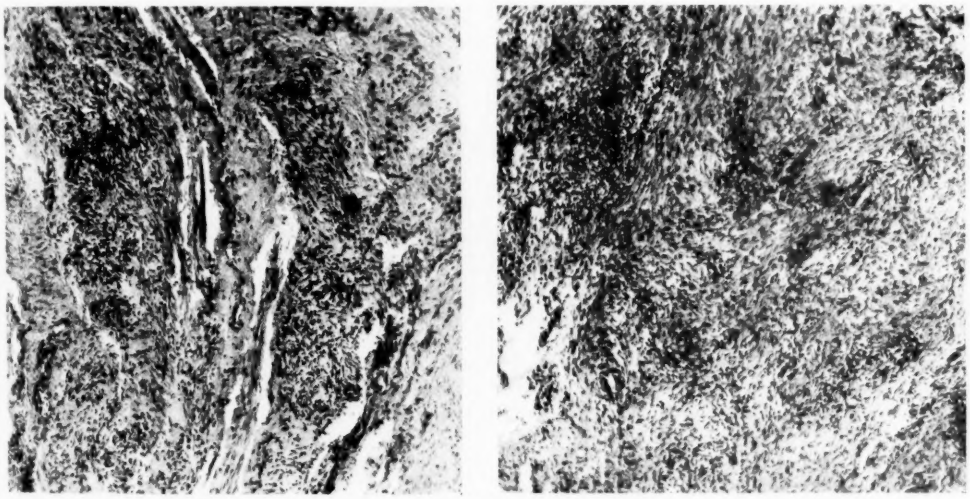

Fig. 2. Two examples of scar tissue (fibroblastic reaction) in bacteriologically negative cases for tubercle bacilli, left, Case 115, and right, Case 139.

to fistula-in-ano before the American Medical Association. After reviewing the literature he asks six questions: (1) What constitutes a tuberculous fistula and on what findings are we justified in making the diagnosis? (2) What percentage of fistulæ are tuberculous? (3) In what percentage of cases is the tuberculous fistula the primary lesion, and in how many cases is it merely a secondary infection from a focus elsewhere in the body? (4) What percentage of fistulæ occurring in tuberculous patients are tuberculous? (5) Does pulmonary tuberculosis have a tendency to cause fistula-in-ano? and, (6) Do simple fistulæ

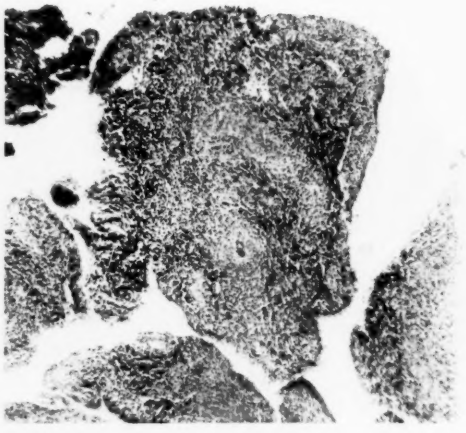

Fig. 3. Two examples of a mild chronic inflammatory tissue reaction. One from a specimen bacteriologically negative for tubercle bacilli, left, Case 25, and the other bacteriologically positive for tubercle bacilli, right, Case 121.

occurring in non-tuberculous persons indicate that the person has a tuberculous tendency? His answers, indecisively given, are based partly on his personal experiences but mainly on conceptions formed from the studies of others. He sums up his beliefs as follows:

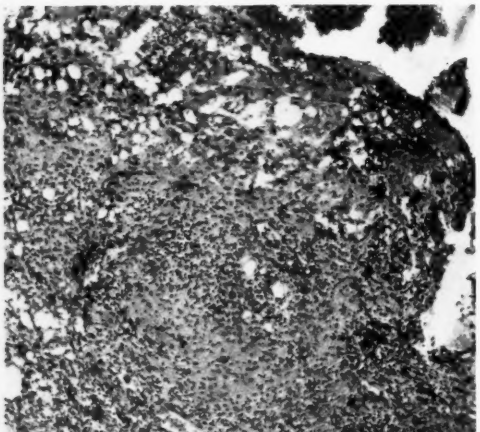

Fig. 4. A typical granulomatous tissue with monocytes and epithelioid cells in a specimen bacteriologically negative for tubercle bacilli, Case 102.

"(1) We are not justified in making the diagnosis of tuberculous fistula except by definite microscopic picture or in cases in which the lesion has the typical appearance. (2) Considering all cases of fistula-in-ano, it is doubtful whether more than 2 or 3 per cent are tuberculous in character. (3) Tuberculosis is very rarely primary in fistula-in-ano. (4) Probably 15 per cent of fistulæ occurring in tuberculous patients are tuberculous; 0.33 per cent of tuberculous patients also have tuberculous fistulæ. (5) In view of the ease with which the tubercle bacillus affects the mucous membrane of the bowel, it would seem possible that in some cases, at least in some persons, in whom the fistulæ appear to be a simple inflammatory process, the original lesion in the bowel wall is due to the tubercle bacilli. However, this is purely a matter of opinion and has not been proved. (6) It is probable that tuberculosis as such has a tendency toward the formation of rectal fistula, and (7) it would seem that the formation of rectal fistulæ in persons who are underweight is undoubtedly a warning of the presence of pulmonary tuberculosis or of a tendency toward its development."

In 1930 and 1931 Petter and Fansler conclude from personal observations reported

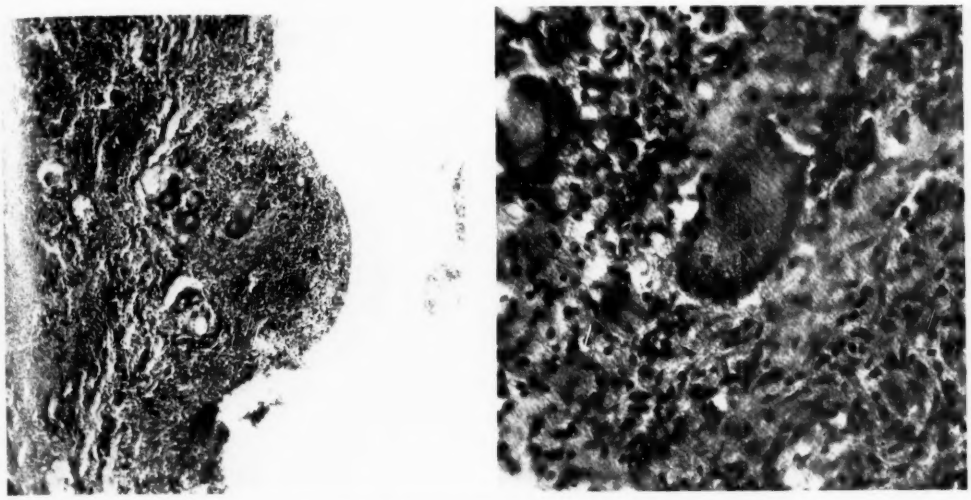

Fig. 5. Giant cells in a specimen from Case 35 bacteriologically negative for tubercle bacilli. Left, low power; right, high power.

from Glen Lake Sanatorium that tuberculous lesions about the anus and rectum occur secondary to a focus elsewhere in practically every case, and that perirectal abscess and fistula-in-ano in the tuberculous patient present a typical history and clinical picture. They found perianal tuberculous skin lesions in 0.8 per cent of patients observed, while perirectal abscess and fistula, in the same group, occurred in 5.8 per cent.

A study of 101 cases of abscess and fistula brought out several important facts; the "proof of tuberculosis" is often quite a task. Smears of exudate are not reliable nor are guinea pigs inoculated with the exudate wholly dependable. A combination of three laboratory procedures gives a reliable "proof of tuberculosis": (1) exudate in guinea pig; (2) macerated tissue in guinea pig, and (3) tissue section. Frequently, tissue section will show a histological picture of chronic inflammation, but not tubercle formation, and a piece of the same tissue injected into the guinea pig will show definite evidence of tuberculosis.

In 1926 Leslie, following a careful study of the literature, concludes that there is still no uniformity of opinion as to the etiological importance of the tubercle bacillus in ischiorectal abscess and fistula-in-ano and suggests that all abscesses and fistulæ in large hospital services be submitted to the following tests; (a) guinea pig inoculation of material from all specimens; (b) a histological study of sections from all cases; (c) a comparative study, following definite diagnosis, of the after history

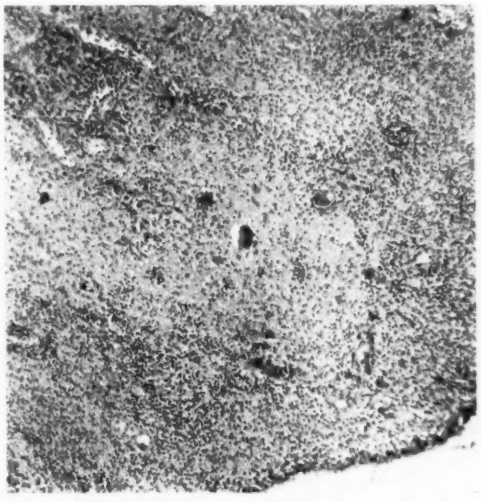

Fig. 6. Giant cell in a specimen from Case 119 bacteriologically negative for tubercle bacilli.

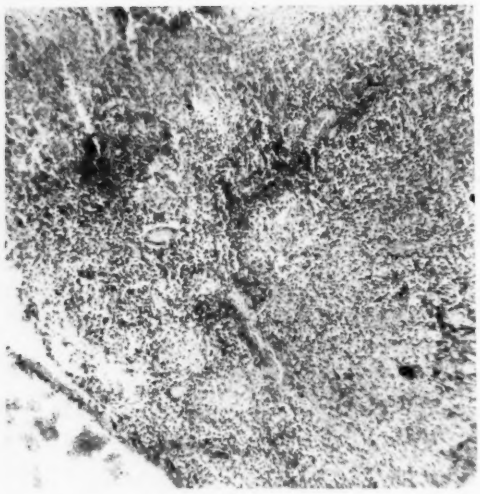

Fig. 7. Giant cells in a specimen from Case 100 bacteriologically positive for tubercle bacilli.

of all cases treated; and (d) more complete examination for tuberculous foci elsewhere.

The same year Clarke, of Belfast, reported his observations on patients with 109 cases of fistula having pulmonary tuberculosis at the Foster Green Hospital for Consumptives and Chest Diseases from which he drew the following conclusions: Ischiorectal abscess and fistula-in-ano occur in males about eight times more commonly than in females—about 5 per cent of male cases of pulmonary tuberculosis are associated at some time with an ischiorectal abscess or a chronic fistula; the fistula or abscess may precede the signs in the lungs by years; there is evidence that 61 per cent of cases of fistula subsequently develop pulmonary tuberculosis; there is evidence that fistula occurs 13 times more commonly in tuberculous males than in non-tuberculous males.

As a result of a study of 150 cases of fistula-in-ano, Tung reported in 1927 that the condition affects people of all classes in China and that hæmorrhoids and tuberculosis were especially noted in the histories. In 102 cases the specimens were examined microscopically and 26, or 25.5 per cent, proved to be tuberculous.

Two important communications have been presented from St. Mark's Hospital which merit citation here. The one was an anatomical study in 1929 by Naunton Morgan, who analyzed 100 cases of peri-ano-rectal infections and found that fistula is three times more common in men than in women; of 196 new cases of fistula during 1928, 146 were men.

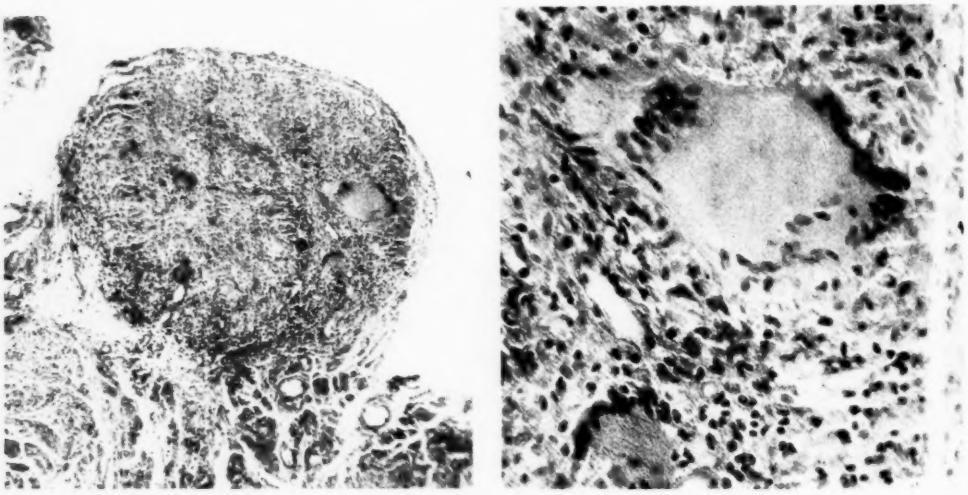

Fig. 8. Classical small tubercle and giant cells in a specimen from Case 52 bacteriologically positive for tubercle bacilli. Left, low power magnification; right, high power showing cells and two typical giant cells.

Anorectal infection was much more common after the age of 30 years, the age of greater frequency being from 30 to 40, the incidence gradually falling off until the age of 60. The condition is more common in children between the ages of 10 and 15 than between the age of 15 and 20. Most fistulæ pass radially into the bowel (46 per cent). Of these more than half are situated in front of a line drawn transversely through the anus (54 per cent). More than half of the ischiorectal abscesses communicate with the bowel and are—or will become—complete fistulæ (56 per cent). A tuberculous fistula will heal well and rapidly, if the patient's general condition is good and there are no signs of active pulmonary disease. Fistula appears to be complicated by pulmonary tuberculosis more frequently in patients over the age of 40 years. In over 60 per cent of the cases there was no definite cause found for the infection; foreign bodies were found in 4 per cent; hæmorrhoids were present in 8 per cent; fissure was present in 7 per cent; inflammation of a crypt was present in 10 per cent. The initial lesion is probably microscopic and is overlooked.

The second and a most important study from St. Mark's which should be considered here, was reported in 1921 by Gabriel and has been frequently and repeatedly cited probably because it is the only detailed bacteriological and histological study of any extent performed to the present time in order to determine the percentage of rectal fistulæ that are tuberculous, the proof required being the definite demonstration or isolation of the tubercle bacillus. The cases investigated were not picked but were taken in succession as admitted into St. Mark's Hospital for operation. Cases of peri-anal abscess were included after discovering the futility of examining the discharge from tuberculous fistulæ in stained films; animal inoculation and histological methods were resorted to. In 30 of the 75 cases guinea pigs were inoculated. Pus, scrapings, and granulation tissue were treated with an equal volume of 15 per cent antiformin after being ground with fine quartz sand and after being diluted with 10 to 20 cubic centimeters of normal saline solution, the sand and larger particles of tissue being allowed to settle, and finally the supernatant fluid being used for antiformin treatment. The antiformin is allowed to act for 5 minutes, with constant shaking, the sediment then obtained by centrifuging is washed with saline and is then injected into the abdominal wall of a guinea pig. After inoculation the animal is kept alive for at least 6 weeks. The antiformin sediment is also examined in smear for bacilli.

Histological examination of the tissue was performed on all of the 75 cases examined, formalin fixation being used for this purpose, paraffin embedding and hæmatoxylin and eosin staining for cellular pathology and cold carbolfuchsin staining with methylene blue counterstaining for tubercle bacilli. Of the 30 cases studied by guinea pig inoculation 6, or 20 per cent, proved positive for tuberculosis, the ages ranging from 21 to 62 years, 5 specimens being from males, and 4 of the 6 showed giant cells in sections while tubercle bacilli were found in none of the stained sections. The 24 negative cases were clinically simple with one exception, a man aged 35 years who had evidence of pulmonary tuberculosis involving both apices, with tubercle bacilli in the sputum. Section from the granulation tissue of the fistula was negative also. Giant cells were found in sections in 2 of the 24 negative cases by inoculation.

In the 45 cases examined only by histological methods, tubercle bacilli were found in the stained sections of 4 (9 per cent) and all revealed characteristic giant cells. Two of these were from men (39 and 49 years of age) with no evident phthisis or pulmonary infection, while the 2 other men (both 18 years of age) had definite pulmonary tuberculosis. One case showed large numbers of giant cells (considered foreign body giant cells) but no bacilli, while of the 40 remaining cases 2 fistulæ were suspicious and showed giant cells but no bacilli. Thirty-eight proved clinically simple, and in 6 of these a few giant cells were found but were considered of no significance by Gabriel, thus leaving finally 32 of the 45 without significant findings for tuberculosis as usually considered. In concluding, Gabriel brings out a few additional points not mentioned above but worth considering: If

histological examination only is carried out, and if no tubercle bacilli are found in sections, a consideration of giant cells can only give a presumptive diagnosis; the absence of giant cells does not exclude the possibility of the tissue being tuberculous.

From a survey of the literature on anorectal fistulæ, it may be questioned whether practically the classification, pathology, or treatment of this condition bears any significance to the bacteriological phases of the condition as is evident from a recent article on this subject by Miles. But a better understanding of the bacteriology and pathology of the condition must inevitably influence the clinician and surgeon's viewpoint as well as that of all those concerned with the health of man, and may eventually entirely change our method of approach in dealing with the condition of anorectal fistulæ.

Since the investigations of the past decade have given us a better insight into the interpretation of tuberculosis and especially has resulted in crystallizing our conceptions regarding the quantitative relations between a positive finding for acid fast bacilli in a smear or section examined microscopically and a positive finding bacteriologically by culture or guinea pig inoculation for tubercle bacilli as contrasted to acid fast bacilli, and since we are better able today to interpret the pathological findings from a practical standpoint as well as quantitative standpoint, it appeared desirable to study more extensively and more accurately the relation of anorectal fistulæ to pulmonary tuberculosis. In initiating this work there were recognized a number of inherent weaknesses in methods available for the so called diagnosis of tuberculosis.

Any method used has its limitations, and these must be fully recognized in interpreting the findings with a certain method. Thus, the finding of acid fast bacilli in a smear or section with the microscope indicates that there are present in the material about 100,000 bacilli per cubic centimeter, while the guinea pig or culture are able to discern as few as 10 to 100 bacilli of a virulent strain of human or bovine tubercle bacilli. The guinea pig or culture when properly used discern only tubercle bacilli and eliminate the saprophytic acid fast bacilli. A precaution in using guinea pigs is to exclude the possibility of spontaneous tuberculous infection which may lead to erroneous conclusions. The quantitative differences between the findings with the smear or section examined microscopically as compared to the guinea pig or culture are particularly significant when we consider that few bacilli can still produce disease and that the reaction may not be of a specific character. It must also be recognized that cellular reactions are significantly non-specific in character and that even the classical giant cell can be produced by a foreign body or by micro-organisms other than tubercle bacilli, and finally tuberculosis can exist without characteristic giant cell formation or tissue reaction and that reactions to the tubercle bacillus are possible, running the entire range from an acute purulent reaction to the formation of dense scar tissue. Add to this the fact that sections, unless serial, which is beyond practical consideration, can only picture the reaction of a very small portion of a diseased tissue and may range from normal tissue to a profound grade of pathology dependent almost entirely on chance.

However, since only a limited series of cases was studied by Gabriel, and since the past 10 years have given us better methods of bacteriological diagnosis and most of all have given us a better conception of tuberculosis it was decided to examine pus, scrapings, and tissues removed from fistulæ-in-ano at operation using every precaution to avoid extraneous contamination and to utilize for examination histological and bacteriological methods and to obtain accurate clinical records regarding especially the status of the patient as concerned tuberculosis. The guinea pigs used in these tests were specially raised for this purpose with all precautions taken to avoid spontaneous tuberculous infection. The culture method used was that previously described from the Research Department of the National Jewish Hospital (3), the oxalic acid crystal violet potato cylinder method. Smears were stained by the usual Ziehl-Nielsen steaming carbolfuchsin methylene blue method while sections were fixed with Zenker's solution paraffin embedded and were

stained with either hæmatoxylin and eosin for cellular study or with carbolfuchsin and methylene blue for acid fast bacilli. Since there is nothing unusual about the methods which have been used except what has been previously recorded for isolating tubercle bacilli, the details will be omitted from this paper so that the pertinent clinical data and histological and bacteriological findings may be presented.

A total of 155 cases were studied in this series, 106 being negative clinically and roentgenologically for evidence of tuberculosis, 18 presenting evidences of arrested pulmonary tuberculosis, and 31 being active cases of pulmonary tuberculosis. None of the cases of pulmonary tuberculosis could be considered to be of the advanced hopeless or fatal miliary type at the time the specimen was obtained for examination. The term active is not intended to convey a last stage case in this sense, but rather to indicate the usual clinical interpretations of activity including physical and roentgenological findings of activity, pyrexia, etc.

In order to evaluate the results of the histological findings they were graded according to the results of an examination of several sections usually taken at several layers in the block of tissue utilized for this purpose. A compromise had to be struck in the case of certain tissues, and they are usually recorded according to the findings of more pronounced grade and pointing to the more marked changes toward a tuberculous tissue. Normal tissues were graded as being negative — "O"; tissues presenting evidences of acute or subacute inflammatory reactions with a predominance of polymorphonuclear leucocytes or granulocytes were graded as "?"; tissues presenting evidences of a chronic inflammatory reaction with scar tissue (connective tissue formation) as the more marked change were graded as "±"; tissues presenting granulomatous changes with the various types of monocytes, clasmatocytes or histiocytes with epithelioid cells and lymphocytes but no

TABLE I.—BACTERIOLOGICAL AND HISTOLOGICAL FINDINGS IN THIRTY-ONE CASES OF ACTIVE PULMONARY TUBERCULOSIS WITH ISCHIORECTAL ABSCESSES OR ANORECTAL FISTULÆ*

Case number	Age Sex	Bacteriological findings (culture and guinea pig)	Histological** findings (sections or smears)	Remarks
7	23 M	+	? pus	F. A.
10	24 M	+	?	M. A. 3 yrs. artificial pneumothorax
11	30 M	+	o	F. A. 4 yrs. myocarditis
13	32 M	+	±	F. A. 4 yrs. pneumothorax
23	29 M	+	? pus	M. A. over 4 yrs.
24	42 M	−	±	F. A. 7 yrs. hæmoptysis
25	22 M	−	±	F. A. 18 mos. hæmoptysis
26	35 F	−	? pus	F. A. 9 yrs.
29	32 M	+	o	F. A. 4 yrs.
30	16 M	+	? pus	M. A. 2 yrs.
31	26 M	+	? pus	F. A. 6 yrs.
36	33 M	+	? pus	F. A. 5 yrs.
41	35 F	+	? pus	F. A. 8 yrs.
55	27 M	+	o	F. A. 4 yrs
56	23 M	−	o	M. A. 4 yrs.
57	16 M	+	±	F. A. 18 mos. hæmoptysis
60	20 F	+	+	M. A. 2 yrs.
73	34 M	+	? pus	F. A. 7 yrs.
77	30 M	+	±	F. A. 5 yrs.
83	29 M	+	?	F. A. 5 yrs.
85	52 M	−	o	F. A. 8 yrs.
86	36 M	+	o	F. A. 3 yrs. pneumothorax
88	32 M	+	o	M. A. 5 yrs.
89	33 F	+	o	F. A. 6 yrs. chronic myocarditis
90	22 M	+	++	F. A. 4 yrs. pneumothorax
95	37 M	+	?	M. A. 7 yrs. pneumothorax hæmoptysis
99	34 M	+	±	F. A. 6 yrs. pneumothorax
109	34 M	+	?	M. A. 3 yrs.
116	36 F	−	o	F. A. 8 yrs. pharyngectomy
132	41 F	−	±	M. A. 4 yrs.
137	24 F	+	±	M. A. 4 yrs. pneumothorax

o means negative; ? means acute cellular reaction; ± means scar tissue; + granulomatous tissues and ++ means tubercles or giant cells.

*In the majority of the cases the pulmonary tuberculosis was moderately (M. A.) or far advanced (F. A.) Most of the patients had anorectal fistulæ.

**Acid fast bacilli were not found in any of the sections stained with carbol fuchsin for this purpose in this series of cases.

TABLE II.—BACTERIOLOGICAL AND HISTOLOGICAL FINDINGS IN EIGHTEEN CASES OF ARRESTED OR INACTIVE PULMONARY TUBERCULOSIS WITH ISCHIORECTAL ABSCESSES OR ANORECTAL FISTULÆ

Case number	Age Sex	Bacteriological findings (culture and guinea pig)	Histological** findings (sections or smears)	Remarks
2	49 M	−	o	Fibroid phthisis 15 years
37	26 M	−	o	Fibroid phthisis 6 years
52	38 M	+	++	Fibroid phthisis 8 years
54	29 M	−	? pus	Fibroid phthisis 8 years
63	32 M	−	?	Fibroid phthisis 6 years
68	31 M	−	?	Fibroid phthisis 5 years
75	25 M	+	++	Fibroid phthisis 5 years
100	24 M	+	++	Fibroid phthisis 3 years
108	50 F	+	?	Fibroid phthisis 10 years
117	34 M	−	o	Fibroid phthisis 7 years
121	41 F	+	±	Fibroid phthisis 8 years
124	50 F	−	?	Fibroid phthisis 17 years
125	34 F	+	o	Fibroid phthisis 6 years
127	45 M	+	+	Fibroid phthisis 10 years
128	27 F	+	o	Fibroid phthisis 8 years
134	32 M	−	o	Fibroid phthisis 7 years
135	29 M	+	o	Fibroid phthisis 7 years
148	24 M	+	o	Fibroid phthisis 4 years

o means negative; ? means acute cellular reaction; ± means scar tissue; + means granulomatous tissues; and ++ means tubercles or giant cells.

**Acid fast bacilli were not found in any of the sections stained with carbolfuchsin for this purpose in this series of cases.

typical giant cells were graded "+"; while tissues containing typical tubercles and giant cells in any part of the section were graded "++." It must always be remembered, however, in evaluating such tissue findings that tubercle bacilli can under certain conditions produce typical acute cellular reactions with a predominance of polymorphonuclear leucocytes or granulocytes and that a typical solitary tubercle sectioned in different places can reveal a variegated picture. These facts combined with the additional fact that giant cells can form around foreign bodies including cellular débris make a diagnosis based on tissue findings alone of uncertain value. All the tissues from the 155 cases were examined for acid fast bacilli after staining with carbol fuchsin but in none were they found in spite of the fact that those presenting the classical tissue picture for tuberculosis were carefully examined although it must be admitted that none of these with giant cells presented profound tuberculous changes with numerous giant cells, such as were described by Gabriel. In the total of 49 cases with active and arrested pulmonary tuberculosis in this series, only 4 presented giant cells and in only 1 of these were they at all fairly numerous. In recording the bacteriological findings, the sum of the culture and guinea pig findings is recorded which in most instances were in accord.

The results of these studies are recorded in Table I for the active cases of pulmonary tuberculosis, in Table II for the arrested cases of pulmonary tuberculosis, and in Table III for the non-tuberculous cases.

An examination of the data recorded in Table I reveals that of the 31 ischiorectal abscesses or anorectal fistulæ occurring in cases of active pulmonary tuberculosis there were 24 specimens in which tubercle bacilli were found by guinea pig inoculation and culture methods while only one (Case 90) revealed tubercle formation or giant cells, another (Case 60) a granulomatous tissue reaction, and in none was acid fast bacilli found in sections of the tissues removed or in smears from the pus obtained from the abscess or fistula.

An examination of the findings recorded in Table II indicates that among 18 inactive cases of pulmonary tuberculosis with ischiorectal abscesses or anorectal fistulæ, there were found 10 cases in which tubercle bacilli were present as determined by bacteriological means (guinea pig and culture test), while only 3 of the 18 (which were also included among the 10 positive by bacteriological methods) revealed tubercle formation or giant cells in

sections and another one, also among the 10 positive bacteriologically, presented granulomatous tissue changes but none was found to contain acid fast bacilli in sections or in smears from the pus obtained from the abscess or fistula.

Now if the bacteriological findings in the inactive, arrested cases of pulmonary tuberculosis are compared with those for the active cases, it is noted that 77 per cent of the active cases were found positive for tubercle bacilli by guinea pig and culture as compared to 55 per cent of the inactive arrested cases of pulmonary tuberculosis. Whether any great significance can be attached to the histological findings obtained in this study in view of all the facts in the case is to be doubted, yet it may be well to call attention to the fact that the giant cell is considered a pathological index of a mild or healing process as contrasted to a leucocytic or monocytic reaction which spells either a progressive or highly active process. The futility of placing too much reliance upon histological findings alone for diagnostic purposes is evident from our present knowledge of the cellular responses to tuberculosis as well as a recognition of the difficulty of examining more than a small portion of tissue by histological and microscopical methods.

The data tabulated in Table III appears to bear out the observations made on tuberculous individuals recorded in Tables I and II in that the histological tissue changes are unreliable as evidence for the presence of tuberculosis in anorectal fistulæ; in 2 of 106 cases the findings were negative by bacteriological methods (with guinea pig and culture test) which revealed in sections typical giant cells, while in 15 of these 106 specimens evidence was presented of a cellular reaction (monocytic, histiocytic, and epithelioid cells) such as occurs in tuberculous conditions but which should not be considered specific for this condition alone. The striking result, however, to be noted from a careful examination of all this data is that tuberculosis of ischiorectal abscesses and anorectal fistulæ is practically limited to individuals with pulmonary tuberculosis evident by clinical and roentgenological examination. The incidence

TABLE III.—HISTOLOGICAL FINDINGS IN ONE HUNDRED AND SIX PATIENTS WITH ISCHIORECTAL ABSCESSES OR ANORECTAL FISTULÆ PROVED NEGATIVE BACTERIOLOGICALLY FOR TUBERCLE BACILLI AND PRESENTING NO CLINICAL OR ROENTGENOLOGIC EVIDENCES OF PULMONARY TUBERCULOSIS

Age in years	Cases
20 to 30	36
30 to 40	29
40 to 50	26
Over 50	15
Total	106
Histological findings*	
Class O	49
Class ?	24
Class ±	16
Class +	15
Class ++	2
Total	106

*The histological findings in these cases are recorded as in Tables I and II; o means tissues examined were normal, ? means tissues presented foci of acute or subacute inflammation with influx of a predominance of granulocytes (polymorphonuclear leucocytes), ± means evidences of connective tissue (scar tissue) reaction, + means evidences of granulomatous infiltration including monocytes and epithelioid cells, ++ means the presence of typical tubercles with necrotic tissue or giant cells.

appears to be slightly less in the favorable inactive or arrested types of pulmonary tuberculosis. It would appear also that the factors which are at play in permitting the invasion of the ordinary pyogenic organisms into the anorectal region and thus favor the production of abscesses or fistulæ in this region also permit the entrance of the tubercle bacillus into these regions, the original sources probably being the pulmonary focus with heavily laden bacillary discharge which, on its course to being discharged from the body, passes over certain predilection sites and, favored by mechanical conditions, results in laryngeal, ileocæcal and rectal localizations, the sites of stasis and frequent mechanical tissue injury permitting entrance, and then a suitable place for abscess formation with its ultimate rupture and fistula. Although the anorectal condition is dependent more or less upon the outcome of the pulmonary condition, rectal hygiene can do much to prevent this condition and proper therapy based on the co-operation of the proctologist and the internist can do a great deal to remove it and prevent recurrences.

SUMMARY AND CONCLUSIONS

As a result of a review of the literature and a bacteriological and histological study of

tissue from ischiorectal abscesses and anorectal fistulæ in a series of 155 cases, in which 106 patients were free from evidences of pulmonary tuberculosis, 18 had an inactive arrested fibroid phthisis, and 31 had an active pulmonary tuberculosis, the following summarized conclusions are presented.

Tubercle bacilli are found by bacteriological methods (guinea pig inoculation and culture tests) in patients with ischiorectal abscesses or anorectal fistulæ only if pulmonary tuberculosis is present; tubercle bacilli were found in 77 per cent of our patients with active and in 55 per cent with inactive (arrested or fibroid) pulmonary tuberculosis but they were not isolated in the 106 cases in which the patients were free from evidences of pulmonary tuberculosis. These findings suggest a close etiological relationship between tuberculous ischiorectal abscess or anorectal fistulæ and pulmonary tuberculosis. Histological methods were found unreliable for determining the tuberculous nature of anorectal conditions except possibly in the presence of marked involvement with typical tubercle formation and the presence of acid fast bacilli which was not a common finding in this series. The presence of giant cells or granulomatous tissue with monocytes and epithelioid cells proved not definitely pathognomonic of tuberculosis in the anorectal region. Acid fast bacilli are not commonly found in sections or smears from tuberculous ischiorectal abscesses or anorectal fistulæ with the aid of the microscope even though they are readily found by reliable culture methods or guinea pig inoculation.

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EXCRETION OF BILE PIGMENTS IN EXPERIMENTAL OBSTRUCTIVE JAUNDICE[1]

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THE question as to whether bile pigments are excreted into the intestinal tract in obstructive jaundice has received but little attention from investigators. Only two references to the subject were found in the literature. Wilbur and Addis while investigating the origin of urobilin, detected traces of this substance in the stools of dogs with common duct occlusion as well as in animals with complete biliary fistula. These workers concluded that urobilin was excreted into the gastro-intestinal tract as such from the blood stream. Wallace and Diamond, in the course of their liver function studies, found small quantities of urobilinogen in the stools of dogs with common duct occlusion and concluded that the urobilinogen originated from bilirubin eliminated into the gastro-intestinal tract from bilirubin saturated plasma.

Our attention was drawn to the subject by the finding of bile pigments in the aspirated stomach contents of a patient with long standing obstructive jaundice. This was interpreted as indicating that the obstruction was not complete and that some communication had been established between the biliary system and the bowel. The question, however, was raised whether the obstruction might not, nevertheless, be complete and the bile staining of the stomach contents be explained on the basis of elimination into the bowel of bile pigments with the gastro-intestinal secretions.

Both Wilbur and Addis and Wallace and Diamond arrived at their conclusions concerning the excretion of bile pigments into the intestinal tract from a study of the stools alone. Apparently neither of these groups of investigators looked higher up in the intestinal tract for bile pigments. It seems logical to suppose that if, in obstructive jaundice, bilirubin is eliminated into the intestinal tract, it should be possible, by examining specimens of stomach and small bowel contents, to detect this pigment before it has been transformed into urobilinogen and urobilin. The following experimental study was undertaken with this in view, namely to produce obstructive jaundice in animals and then: (1) to study the bile pigment content at various levels in the gastro-intestinal tract and (2) to study the relationship of the elimination of these pigments (a) in the bowel and (b) in the urine, to the level of blood bilirubin concentration.

EXPERIMENTAL PROCEDURE

Dogs were used for all experiments. The animals were kept in metabolism cages and fed on a mixed diet. Operations were performed with aseptic technique, under ether anæsthesia. After a preliminary period of 1 or 2 days during which the blood, urine, and stools were examined for bile pigments, the common duct was ligated and resected about 1 inch from the duodenum in 16 animals. In 6 others a cholecystectomy was performed in addition to the common duct ligation. The stools were thereafter examined each day for bilirubin, urobilinogen, and hydrobilirubin. Blood bilirubin and urine bilirubin determinations were made daily.

During the earlier part of this work, 4 of the animals were explored after they had developed a pronounced generalized icterus. The biliary ducts were inspected to verify the absence of any communications with the bowel. Specimens of the contents of the bowel were removed through small incisions in the stomach, small bowel, and proximal colon and examined for bilirubin and urobilinogen. This practice was, however, discontinued because 3 of the animals expired during the operation and 1 several hours afterward. Since the operation occasioned little surgical trauma and very little loss of blood, we attributed the cause of death to the anæsthetic. Ether had been used for 2 animals and nembutal, in minimal doses for surgical anæsthesia (25 milligrams per kilogram body weight, given intravenously), proved equally fatal in the 2 others. The remaining

[1]From the Gall Bladder Group, Michael Reese Hospital and the Department of Chemistry, Nelson Morris Institute. Aided by a grant from the Gusta Morris Rothschild Fund.

animals were explored only after death, when specimens were taken from the stomach, small bowel, and colon. At necropsy each animal was examined to verify the completeness of the occlusion of the common duct and to ascertain the absence of anomalous communications between the biliary channels and the bowel. The method of obtaining specimens from the bowel was as follows: The bowel was incised and gross particles of food, if present, were discarded. The material in the bowel was removed with a dull porcelain spoon, care being taken not to scrape the mucosa. In some animals the bowel contained so little material, that rather than risk scraping the mucosa, a segment of the bowel was rolled longitudinally and the contents gently expressed.

The chemical methods employed were:

I. Fæces: (1) Schmidt's test for hydrobilirubin. (2) Huppert's test for bilirubin. (3) Urobilinogen was determined according to the method described by Wallace and Diamond.

II. Gastro-intestinal contents: in addition to those enumerated above, the following test for bilirubin was also used:

To about 10 grams of the fresh material to be examined, 25 cubic centimeters of 0.1 per cent potassium hydroxide is added and the mixture vigorously shaken for several minutes, and centrifuged. To 2 cubic centimeters of the supernatant fluid, 2 cubic centimeters of the hydrochloric acid-sodium nitrate[1] reagent described below is added. In the presence of bilirubin the solution will turn green. This test is an adaptation of the quantitative urine bilirubin method described by Sabatini. We found this test much more sensitive than any of the other qualitative tests. Unlike the van den Bergh, this test is specific for bilirubin since the development of the green color depends upon the oxidation of bilirubin to biliverdin.

III. Blood: Blood bilirubin was determined by the quantitative van den Bergh method. The standards described by van den Bergh are not of exactly the same shades as those produced in the serum. Nichols and Jackson have described standards with more comparable colors. Comparison is made grossly against a series of standards in a comparator box. We have found this method adequate for the determination of variations of blood bilirubin concentration, that exceed 1 milligram per 100 cubic centimeters. For the determination of changes of less than 1 milligram we have employed the micro-colorimeter, with the same standards of Nichols and Jackson.

Experimental results. Excretion of bile pigments into the gastro-intestinal tract.

Fæces. Tests for *bilirubin* were always negative in the stools of all animals. Tests for *hydrobilirubin* became totally negative in all cases after the second to the fourth day after operation, and remained so until death. Frequently no trace of hydrobilirubin could be detected during the preliminary period in normal dogs. We gained the impression that Schmidt's test for hydrobilirubin is of very little use in the detection of bile pigments in the stool, though it is widely used by clinicians for this purpose.

The stools were always positive for *urobilinogen* in the preliminary period but in most experiments this substance began to disappear about 3 to 6 days after occlusion of the common duct. After the seventh post-operative day the stools remained constantly negative for urobilinogen until death, in 16 of the 22 animals. Traces of urobilinogen were found constantly in the fæces of 3 (Nos. 13, 19, and 21) of the 6 remaining. In the 3 others (Nos. 7, 10, and 23) urobilinogen disappeared from the fæces for periods of 26, 23, and 24 days, respectively. The urobilinogen thereafter reappeared in these cases in the stools and persisted until death. The blood bilirubin in these, at the time when urobilinogen began to appear in the stools, was 54, 30, and 28 milligrams per 100 cubic centimeters, respectively.

Of the group that was constantly positive for urobilinogen, at autopsy, one (No. 19) had a gastric ulcer, another (No. 13) had diffuse ecchymotic areas in the mucosa of the large bowel, and the third (No. 21) exhibited nothing unusual apart from the marked generalized icterus and markedly engorged bile

[1]Solution 1. Concentrated hydrochloric acid, 12 c.cm. Water to 100 c.cm.
Solution 2. 1% sodium nitrite.
To 30 c.cm. of solution 1, add 1 c.cm. of solution 2. This reagent must be prepared only as required, since it deteriorates after several hours.

TABLE I.—EXCRETION OF BILE PIGMENTS INTO THE GASTRO-INTESTINAL TRACT IN EXPERIMENTAL OBSTRUCTIVE JAUNDICE

Animal number	Days after operation	Blood† bilirubin mgs. per 100 c.cm.	Stomach		Small intestines		Colon		Fæces			Remarks
			Bilirubin	Urobilinogen	Bilirubin	Urobilinogen	Bilirubin	Urobilinogen	Bilirubin	Urobilinogen	Hydrobilirubin	
3	18	12	mg.	o	o	o	o	o	o	o	o	Explored on 18th day; expired after operation
4	14	6	o	o	o	o	o	o	o	o	o	Explored on 14th day; expired after operation
6	9	23	o	o	o	o	o	o	o	o	o	Cholecystectomy
7	72	54	Trace	o	++	Trace	o	++	o	++	o	Necropsy: Ascites, cirrhosis of liver. Stools positive for urobilinogen for 40 days before exitus
8	18	20	o	o	o	o	o	o	o	o	o	Cholecystectomy
9	22	14	o	o	o	o	o	o	o	o	o	
10	43	30	o	o	+	o	o	+	o	+	o	Stools positive for urobilinogen for 15 days before exitus
12	20	14	o	o	o	o	o	o	o	o	o	
13	36	26	o	o	+	o	o	+	o	+	o	Urobilinogen constantly present in stools. At necropsy ecchymotic areas in mucosa of bowel
15	19	15	o	o	o	o	o	o	o	o	o	Explored on 18th day and expired on following day
17	18	15	o	o	o	o	o	o	o	o	o	
18	20	20	o	o	o	o	o	o	o	o	o	Cholecystectomy
19	30	23	o	o	+	o	o	+	o	+	o	Traces of urobilinogen in stools, constantly present. At necropsy, gastric ulcer
20	20	19	o	o	o	o	o	o	o	o	o	
21	34	26	o	o	+	o	o	+	o	+	o	Cholecystectomy. Traces of urobilinogen constantly in stools
22	36	24	o	o	+	o	o	Trace	o	o	o	
23	38	28	o	o	+	o	o	+	o	+	o	Stools positive for urobilinogen for 9 days before exitus
24	24	15	o	o	o	o	o	o	o	o	o	
26	21	16	o	o	o	o	o	o	o	o	o	
28	10	14	o	o	o	o	o	o	o	o	o	Cholecystectomy
29	23	16	o	o	o	o	o	o	o	o	o	
30	18	28	o	o	o	o	o	o	o	o	o	Cholecystectomy

† These represent specimens drawn within 24 hr. before exitus.

passages. The constant presence of urobilinogen in the stools of Nos. 19 and 13 is probably attributable to hæmorrhage into the bowel. With hæmorrhage bilirubin is introduced into the bowel which would account for the urobilinogen in the stools. No. 21 remains a puzzle. The possibility of bile entering the intestinal tract through some aberrant bile duct as well as the existence of some lesions in the gastro-intestinal tract which might account for hæmorrhage into the bowel were excluded at autopsy.

GASTRO-INTESTINAL SECRETIONS

The specimens removed from the group of 4 jaundiced animals that were explored under ether and nembutal anæsthesia were all negative for bilirubin and urobilinogen. The results of the remaining 18 that were examined after death are summarized in Table I.

Traces of bilirubin were found in the stomach of only 1 animal (dog 7), in the small bowel of 7 animals, and in the colon of none. Of the 7 that had traces of bilirubin in the small bowel, the stools of 6 were positive for urobilinogen before death. Urobilinogen was found in the colon of all cases, in the small bowel of which bilirubin had been found.

No urobilinogen was ever detected in the stomach and only once in the small bowel (No. 7). Dog 7 presented two unusual features—presence of bilirubin in the stomach and of urobilinogen in the small bowel. This animal presented other interesting features that merit recording. The animal lived for 72 days with a complete obstruction of the common duct. At necropsy, the peritoneal cavity contained 110 cubic centimeters of clear amber colored ascitic fluid. This fluid contained 40 milligrams of bilirubin per 100 cubic centimeters, but no urobilinogen. The gall bladder was distended to about five times its normal size. The liver was cirrhotic.

DEDUCTIONS FROM EXPERIMENTS

On studying the experimental results summarized in Table I, certain facts are noted.

1. If an animal survives long enough after a common duct occlusion, bile pigments will appear in the gastro-intestinal tract. Bile pigments were found in the intestinal contents of all animals that lived more than 30 days after the experimental obstruction, and none was found in the intestines of animals who survived for a shorter period.

2. Urobilinogen can be detected in the stools of animals with complete obstruction of the biliary ducts if the obstruction is of long duration. After death, bilirubin was found in the small bowel of all these animals, the stools of which had been positive for urobilinogen. In 1 animal (No. 22), with stools negative for urobilinogen, traces of bilirubin were found in the small bowel and of urobilinogen in the colon. Since it is a well established fact that urobilinogen is absorbed from the intestines, the absence of urobilinogen from the fæces in this case is probably accounted for in this manner.

3. The blood bilirubin concentration must attain a certain level before bile pigments will be excreted into the bowel. The blood bilirubin concentration exceeded 22 milligrams per 100 cubic centimeters in all animals that had bile pigments in their intestines. It seems, however, that the blood bilirubin concentration is not by itself the determining factor in the elimination of bilirubin into the bowel, since, in one animal (No. 30) the blood bilirubin rose to 28 milligrams before death and no bilirubin or urobilinogen was found in its gastro-intestinal tract, whereas, three other animals were eliminating bile pigments into the intestinal tract at lower blood bilirubin levels (No. 13 at 26 milligrams; No. 21 at 26 milligrams; No. 22 at 24 milligrams). The degree of saturation of the tissues with bile pigments is probably the deciding factor in the elimination of these pigments into the intestinal tract.

4. Certain pigments are found only in certain portions of the bowel which are anatomically and physiologically distinct from each other. With but one exception in the entire series, bilirubin was found only in the small bowel and urobilinogen only in the colon.

The absence of bilirubin from the colon and urobilinogen from the small bowel is in agreement with the commonly accepted theory of urobilinogen formation. The bilirubin in the bowel is believed to be reduced by bacterial action to urobilinogen. While this process may take place to some extent in the lower part of the small bowel, in only 1 case (No. 7) was urobilinogen detected here.

URINE BILIRUBIN EXCRETION

The second part of this experimental work concerns itself with a quantitative study of the relationship of blood bilirubin concentration to bilirubin excretion in the urine. Since Mann and his co-workers (1) have shown that the bilirubin content of arterial blood is the same throughout the body, while the bilirubin content of the blood of the accessible veins varies, all blood specimens were obtained from the femoral artery except where otherwise indicated.

Method. The colorimetric method of Sabatini was used to determine the bilirubin concentration in the urine. The method consists

TABLE II.—BLOOD BILIRUBIN CONCENTRATION AND URINE BILIRUBIN EXCRETION FOLLOWING COMMON DUCT LIGATION.*

Date	Days after operation	Blood bilirubin mgs. per 100 c.cm.	Urine volume in cc. per 24 hr.	Urine bilirubin mgs. per 100 c.cm.	Urine bilirubin mgs. per 24 hr.
11–16 to 11–17†	Preliminary period	0	250	0	0
11–18	1	1	220	Trace	Trace
11–19	2	1.5	350	2.5	9
11–20	3	2	300	4	12
11–21	4	2.5	285	5.5	16
11–22	5	2.5	330	6	19
11–23‡	6	3	250	8	20
11–24§	7	3.0	260	8.5	24
11–25	8	4.0	320	9	29
11–26	9	4	310	10	31
11–27‖	10	4.5	330	10	31
11–28	11	4.5	346	10.5	36
11–29	12	5	332	12	40
11–30¶	13	5.5	340	13.5	46
12–1	14	6.5	360	15	54
12–2	15	6.5	350	16	56
12–3	16		310	19	59
12–4**	17	7	318	20	64
12–5	18	7.5	260	26	68
12–6	19	8.5	350	27	94
12–7	20	8.5	300	33	99
12–8	21	9	483	21	101
12–9	22	10	542	26	141
12–10	23	12.5	760	23	175
12–11	24	15	2000	11	220
12–12††	25				

*Female dog, No. 24, weight 15 kilograms.
†Common duct ligated and severed. Ether anæsthesia. Operation, 11–17–31. ‡Weight 11.5 kilograms. §Wound infection. ‖Wound resutured. ¶Weight 9.5 kilograms. **Wt. 7 kilograms. ††Exitus.

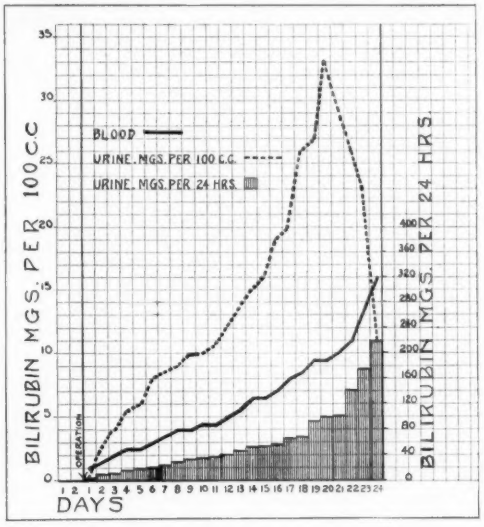

Fig 1. Relationship of blood bilirubin concentration to urine bilirubin concentration and output in milligrams per hour following experimental obstructive jaundice.

in the oxidation of bilirubin by a hydrochloric acid-sodium nitrite mixture to biliverdin with the formation of a green color. This color is then compared in a colorimeter with an artificial standard (a mixture of chrome alum and potassium dichromate), representing a concentration of bilirubin of 1:10,000. Although the author fails to mention it, the colorimetric standard can only be used with daylight since artificial light brings out a reddish phosphorescence in the standard. Specimens of urine should be examined while fresh, since a certain amount of bilirubin disappears from the urine on standing at room temperature. Specimens can, however, be kept in the refrigerator for 12 hours without the loss of appreciable amounts of bilirubin. Urines which have undergone ammoniacal decomposition yield colors which cannot be compared with the standard. Particular care should be taken to keep the urine clear of fæces. Particles of fæces soaking in the urine will interfere with the development of the characteristic green color.

In the experiments the specimens were collected immediately or shortly after voiding, and filtered. The bilirubin determination on the specimen was then performed immediately. If the animal voided in the evening a few drops of toluene were added and the specimen placed in the refrigerator and examined in the morning. At the end of each 24 hour period the animals were catheterized.

The color of the urine after the addition of the reagent at times did not exactly match the shade of the standard. This was more noticeable in urines of low bilirubin concentration (3 to 5 milligrams per 100 cubic centimeters). Urines containing concentrations of bilirubin

TABLE III.—BLOOD BILIRUBIN CONCENTRATION AND URINE BILIRUBIN EXCRETION FOLLOWING COMMON DUCT LIGATION AND CHOLECYSTECTOMY.*

Date	Days after operation	Blood bilirubin mgs. per 100 c.cm.	Urine volume cc. per 24 hr.	Urine bilirubin mgs. per 100 c.cm.	Urine bilirubin mgs. per 24 hr.
12–2 to 12–3†	Preliminary period	0	400	0	0
12–4	1	5	450	40	180
12–5	2	20	425	57	242
12–6‡	3	30	400	66	263
12–7	4	18.0	352	54	190
12–8	5	16	266	71	189
12–9	6	16	268	70	188
12–10	7	18	250	80	200
12–11	8	20	220	93	205
12–12¶	9	23	205	112	229
12–13§					

*Female, dog 6, weight 12 kilograms. †Operation, 12–3–31. Common duct ligated and severed and cholecystectomy. Ether anæsthesia. ‡Weight 10.5 kilograms. Abdominal wound infection. ¶Weight 7 kilograms. §Exitus.

above 10 milligrams per 100 cubic centimeters always yielded shades comparable to, if not identical with, the standard. While the method will not enable one to measure quantitatively the traces that occur in the urine below concentrations of 3 or 4 milligrams bilirubin per 100 cubic centimeters of urine, it is adequate for the quantitative measurement of the variations in bilirubin concentrations that occur in the urine following common duct occlusion.

Experimental results. The results of a typical experiment following common duct occlusion are given in Table II (Fig. 1). The gradual rise in blood bilirubin is paralleled by corresponding increases in the bilirubin excretion. Table III shows the more rapid rise of bilirubin in both blood and urine which occurs when a cholecystectomy is performed in addition to occlusion of the common duct. If the gall bladder is allowed to remain, it seems to act as a reservoir for bile, leading to a slow, gradual rise in the blood bilirubin. In 2 of the 6 animals upon which cholecystectomies were performed, there occurred a rapid rise in blood bilirubin (Table III), followed by a falling of the blood values for several days, and in turn

TABLE IV.—BILIRUBINÆMIA AND BILIRUBINURIA DURING FIRST SEVEN HOURS OF COMPLETE COMMON DUCT OBSTRUCTION.*

Specimen	Time after operation	Blood Bilirubin mgs. per 100 c.cm.		Urine bilirubin mgs. 100 c.cm.	Urine volume c.cm. per hr.	Urine bilirubin mgs. per hr.
		Arterial	Venous			
1†	Preliminary period	Negative	Negative	0	12	0
2‡	30 min.	.25	.25	Trace	15	?
3	60	1	1.25	5	12	.6
4	90	2	2.2	7.5	11	.8
5	120	2.5	2.5	10	12	1.2
6	150	3.0	3.0	10	11.5	1.0
7	180	3.5	3.75	14	10	1.4
8	210	4.5	4.5	20	8	1.6
9	240	5.5	5.5	30	8	2.4
10	270	6.0	6.0	42	6	2.5
11§	300	6.5	6.75	8	35	2.8
12	330	7.0	7.0	Trace	52	?
13	360	7.5	7.5	7.5	25	1.8
14	390	7.5	7.8	14.5	12	1.7
15	420	8.0	8.00	25	10	2.5
16	450	8.0	8.00	38	8	3.0

*Remarks. Female, weight 14 kilograms.
†Catheterized and catheter held in place with a suture. Right femoral artery and vein exposed.
‡Common duct ligated and resected under ether anæsthesia.
§250 c.cm. 10 per cent glucose intravenously.

by a steady rise until death. Urine bilirubin values paralleled the blood bilirubin fluctuations. The maximum value for blood bilirubin observed was 54 milligrams in dog 7, and occurred 72 days after common duct occlusion. The corresponding urine bilirubin concentration in the same animal was 220 milligrams per 100 cubic centimeters. This is a ratio of blood bilirubin to urine bilirubin concentration of 1:4. The highest ratio (1:8) occurred in dog 6. Blood bilirubin was 5 milligrams and the corresponding urine bilirubin 40 milligrams per 100 cubic centimeters. The curves of blood and urine bilirubin concentration did not always run parallel. The rate, however, of bilirubin excretion always paralleled closely the variations in the blood bilirubin concentration (Fig. 1).

In Table IV are given the results of an experiment in which arterial and venous blood and urine specimens were collected at half

hourly intervals. In order to ensure the simultaneous collection of arterial and venous specimens the femoral artery and vein were exposed. Mann and his co-workers (1, 2) using a spectrophotometric method for the determination of bilirubin, reported higher blood bilirubin concentration in the femoral vein than in the blood drawn simultaneously from the femoral artery. We were never able to demonstrate differences of greater magnitude than 0.5 milligram between arterial and venous samples and these, not constantly. It is significant, however, that when differences were detected, the venous blood values were always higher than the arterial.

In 3 animals, several days before death, a drop in the blood bilirubin values and a corresponding fall in the bilirubin excretion occurred, which continued until death (Table V). Postmortem examination of these animals revealed nothing to explain the terminal drop in blood and urine bilirubin. The common duct occlusion was complete in each case and no anomalous communications between the bile passages and the bowel were found.

TABLE V.—TERMINAL FALL IN BLOOD BILIRUBIN CONCENTRATION AND URINE BILIRUBIN EXCRETION FOLLOWING COMMON DUCT LIGATION.*

Date	Days after operation	Blood bilirubin	Urine volume per 24 hr.	Urine bilirubin mgms. 100 c.cm.	Urine bilirubin mgms. 24 hrs.
11–6† to 11–7	Preliminary period	0	200 c.cm.	0	0
11–8	1	2	170	5	8.5
11–9	2	2.5	220	8	18
11–10	3	3.5	230	9.5	22
11–12	4	4	210	11	23
11–13	5	5	222	12	27
11–14	6	5.5	190	14.5	28
11–15	7	6.5	204	14	29
11–16	8	7	178	17	30
11–17	9	7.5	132	22	29
11–18	10	7.5	206	16	33
11–19	11	6	133	21	28
11–20	12	5.0	170	15	26
11–21	13	3.5	158	12	19
11–22‡	14	3.0	Incomplete	9.5	

*Female, dog 4, weight 9 kilograms.
†11–7, ether anæsthesia. Common duct ligated and resected.
‡Exitus. Necropsy: Complete occlusion of common duct; no anomalous bile ducts. Generalized icterus. Gall bladder distended to about twice its normal size.

CONCLUSIONS

1. In complete obstructive jaundice of long duration in dogs, bile pigments are eliminated into the gastro-intestinal tract, and can be detected as bilirubin in the small bowel and urobilinogen in the large bowel. Urobilinogen can be found in the stools of the same animals, although Schmidt's hydrobilirubin test which is widely used clinically for the detection of bile pigments in fæces was constantly negative.

2. The elimination of bile pigments into the bowel seems to be determined by a combination of factors: (A) The blood bilirubin concentration (23 milligrams per 100 cubic centimeters of blood was the lowest blood bilirubin level at which bile pigments were found in the intestinal tract). (B) The duration of the complete biliary obstruction. (Bile pigments were never detected in the intestinal tract of animals who lived for less than 30 days after the common duct occlusion.)

3. There is a close parallelism between the blood bilirubin concentration and the rate of bilirubin excretion by the kidneys following experimental obstructive jaundice.

The author wishes to express his thanks to Dr. Ralph B. Bettman whose interest made this work possible and to Dr. David J. Cohn for many helpful suggestions with the chemical methods.

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PYELOMETRY

A Graphic Study of the Contractions of the Kidney Pelvis[1]

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IN former communications, the author has drawn attention to the study of the normal and pathological physiology and pharmacology of the kidney pelvis by means of pyeloscopy and of pyelometry in both the human being and in the experimental animal. In the present communication some results of the pyelometrical study of the kidney pelvis in the human being are submitted. The scope of the inquiry is, of course, limited by the material and facilities available; in all cases the observations recorded by pyeloscopy, pyelography, and pyelometry were studied in association with the clinical findings. Obviously in the human being the study of the action of drugs was limited by the pharmacological requirements of the case and the therapeutic indications as suggested by animal experiments (3).

With the conscious assistance of the patient the effects of various procedures could be investigated such as: sitting up, lying down, lying on the affected side, lying on the opposite side, coughing, deep respirations, Valsalva's experiment (forcible expiratory effort with closed glottis at the end of inspiration), and alterations of posture by altering the inclination of the table on which the patient lay.

METHOD

A ureteric catheter as large as possible up to 7 or 8 Charrière was passed into the pelvis of the kidney. The position of the eye of the catheter was verified by examination under the fluorescent screen and the filling of the kidney pelvis with abrodil or uroselectan B solution was carried out under direct vision through the screen. The kidney pelvis being filled its contractions were observed and the passage of the "globule" down the ureter alongside the inlying catheter observed. (This was obviously not a normal state of affairs but the findings could be verified by subsequent pyeloscopy after removal of the catheter.)

It is recognized that the presence of an abnormal fluid in the kidney pelvis is not a normal state of affairs and that the injection of this fluid into the pelvis through the inlying ureteric catheter also introduces an unknown factor, but, until pyeloscopy is possible with the dye in the pelvis excreted there by the kidney after oral administration or parenteral injection such as is done in intravenous pyelography the method must stand.

The kidney pelvis was then emptied of abrodil and washed out with normal saline and then connected up as illustrated in a previous paper (2, Fig. 1).

Drugs investigated were injected subcutaneously or intramuscularly. It is recognized that the intravenous route would be experimentally more desirable, but this is not always clinically expedient. Again the drugs were used only in therapeutic doses and so the human being of 50 kilograms would receive intramuscularly or subcutaneously the same dose of such drugs as pituitrin, eserine, strychnine, atropine as the dog of 8 to 10 kilograms received intravenously and in the case of histamine and morphine a smaller dose. This may account for some of the differences noted.

RESULTS OBTAINED

In all tracings upward movement indicates contraction and downward movement relaxation. Time: 90 mm = 1 minute. *The normal tracing.* The apparently normal tracing (Fig. 1) shows a series of small waves, generally 2, 3, or 4 in number, superimposed on larger waves—generally on the ascending limb of the wave, but sometimes on the descending limb. I take these small waves to indicate contractions of the calyces while the large wave indicates contraction of the pelvis itself ("ventricle"). The rhythm is regular and the height of the contractions more or less constant.

1. *Effects of posture in the normal.* (a) Sitting up causes a marked and rapid rise in

[1] From the Gynæcological and Radiological Departments of the Women's Hospital, Melbourne.

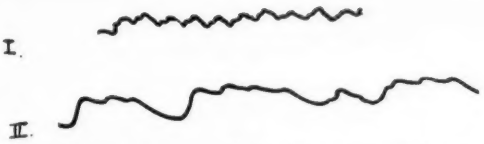
pressure up to a maximum, when the tracing maintains a plateau. It sometimes, however, gradually falls after reaching maximum level. In the latter case I take it that the urine under pressure in the pelvis is escaping *alongside* the catheter and so the pressure falls (Fig. 2).

b. On lying down, after a momentary slight rise in pressure due perhaps to muscular effort, the pressure falls rapidly to normal (Fig. 2). The same effects were produced by raising the head of the table and then restoring the patient to the horizontal without any apparent conscious effort on the part of the patient.

2. *Increased intra-abdominal pressure* induced by muscular movement, coughing, laughing, Valsalva's experiment all produce a rise in pressure in the kidney pelvis which is what one would expect (Fig. 3). If the patient is made to sit up first, and then told to strain, cough, or Valsalva, there is a further rise superimposed on the first rise, and this second is often as great as that induced by the same procedure with the patient lying down. With a small inlying catheter, if these procedures are repeated several times in quick succession the response becomes less. I think this is due to the emptying of the pelvis down the ureter alongside the catheter.

3. *Effect of drugs in the normal.* Histamine in the doses given (grain 1/22 to grain 1/44) injected intramuscularly, induces contraction of the kidney pelvis (Fig. 4).

Atropine apparently causes contraction in the experimental animal (dog) (2), although in the human being relaxation is generally seen, but sometimes a contraction is obtained (Fig. 5). Apparently this effect is due to cutting out of vagal action (3).



All tracings are comparable, the time relations being the same and are all drawn to the same scale (1 to 1) from the original tracings.

Fig. 1. Normal tracing. *I*, Mrs. B. Note calycinal contractions on upstroke, i.e., during systole of the pelvic "ventricle." *II*, Mrs. D. Note calycinal contractions on the downstroke, i.e., during diastole of the pelvic ventricle. The difference in rate of ventricular contraction may have a bearing on this.

Pituitrin generally produces a rise with "flattening" of the wave and obliteration of the rhythmic contractions.

Eserine causes contraction although this is generally better seen pyeloscopically than graphically. It was also noticed that after eserine a much greater contraction was obtained when the patient sat up than was obtained before eserine was injected (Fig. 6).

In pathological cases. (a) In mild degrees of hydronephrosis (capacity of pelvis 15 to 20 cubic centimeters), the tracing obtained showed very shallow waves.

1. *Effects of sitting up.* The rise induced by sitting up was very much less than in the normal. When, however, this procedure was repeated several times, a higher and higher response was obtained *with relief* of pain and the contractions of the calyx were better and larger. This confirms what one finds on pyeloscopy. This type of pelvis will be seen to contract well when nearly emptied and with

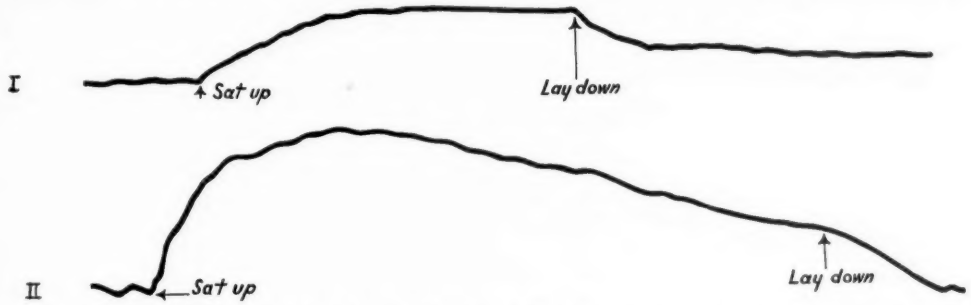


Fig. 2. Effects of sitting up and lying down (see text). *I*, Mrs. McL., same patient as in Figure 9 but normal (opposite) side. *II*, Mrs. D., same patient as in Figure 1, tracing *II*.

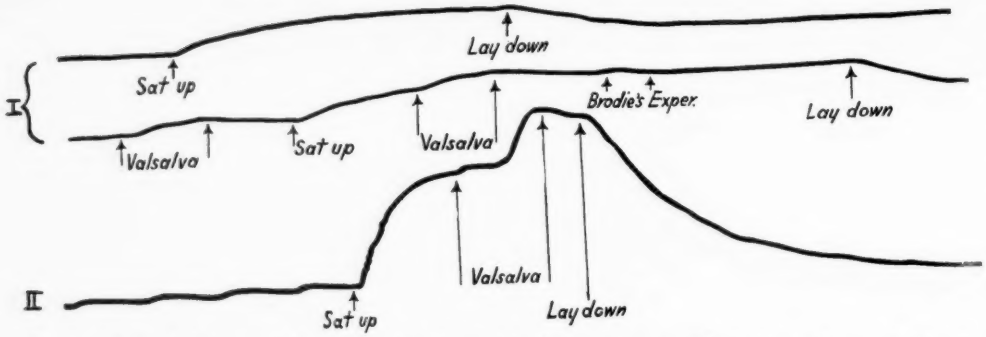


Fig. 3. Effects of sitting up, lying down, raising intra-abdominal pressure by Valsalva's experiment. *I*, Mrs. B., normal case. Small catheter. Calycinal contractions not shown. *II*, Mrs. W., slight dilatation of pelvis (capacity 15 cubic centimeters).

only 2 or 3 cubic centimeters abrodil solution run in. When, however, 15 or 20 cubic centimeters are run in the contractions are poor and the patient may complain of discomfort. Apparently the effect of sitting up and lying down several times in quick succession is practically to empty the overfilled pelvis with relief of pain.

2. *Effects of drugs.* Pituitrin appears to increase the tone in these cases without much increase in intrapelvic pressure as a result of the drug (Fig. 7). This is seen in the more marked response to sitting up than was seen before, whereas in other cases a smaller response is obtained owing to the pelvis already being in a state of contraction.

In cases of dysfunction—irregular contractions associated with pain (Fig. 8). 1. *Effect of posture.* In some cases after the rise induced by sitting up, the contractions become regular and pain is relieved (Fig. 8).

2. *Effects of drugs.* Pituitrin in these cases often does not produce so much a rise in intrapelvic pressure as a steadying of the pelvic contractions with production of regular waves (Fig. 8). In all cases of irregular contractions with pain wherever the irregularities were corrected by posture or drugs the pain was relieved. With the return of the arrhythmia, the patient complained of pain once more.

RESULTS

The results so far obtained encourage one in the hope that the graphic method may give us information which can be studied at leisure and collated with pyelographic, pyeloscopic, and clinical findings. The effects of posture are at first rather startling and will explain the beneficial results obtained by posture in some cases of pyelitis and in some cases of kidney pain. The apparent benefit derived from massage of the kidney region in some cases can also be understood when it is borne in mind that this massage may induce a rise in the intrapelvic pressure which would facilitate emptying of the pelvis and assist in overcoming slight spasm in ureter or pelvi-ureteral junction.

In regard to the action of drugs, as a rule the results obtained in the experimental animal (2) were confirmed but in some cases one obtained an apparent reversed action, but

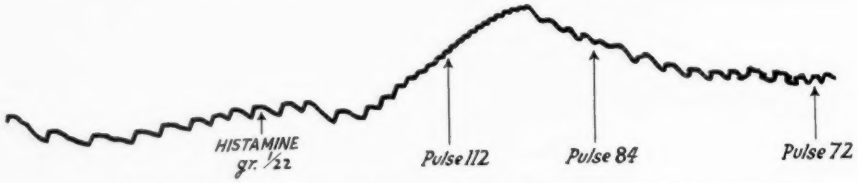


Fig. 4. Action of histamine injected intramuscularly. Mrs. B. Compare Figure 1, tracing *I*.

hether this was due to the well known phe-omenon of the reversed action of smaller ose or to the inherent difference in reaction f the human being and the dog to these par-cular drugs has not so far been fully investi-ated, but such experimental observations as ere made suggested the former.

This was particularly the case with atropine and with histamine. Atropine in the doses given gave an apparent contraction of the pelvis in some cases, but this contraction may have been secondary and due to cutting out of vagal action. In other cases relaxation of the pelvis with overfilling and consequent pain was obtained.

With regard to histamine a very definite rise in pressure was obtained in most cases with the doses given.

In neurotic women and women who were the subjects of spasm in the ureter or dysfunction of some kind as observed by pyeloscopy, it was seen that the normal contractions of the pelvis and calyces were much shallower than normal and sometimes hardly apparent. In these cases pituitrin, eserine, and strychnine often failed to produce any further contraction so that the pelvis was apparently in a condition of hypertonic contraction. In these cases quinine grains, 5 given 3 times a day, generally caused relaxation (3) and relief of pain. The pyelo-ureterogram of such a patient is illustrated (Fig. 9). After a course of quinine she is now apparently quite well and free from pain.

In other cases (Fig. 8) also the tracing showed an irregular series of waves accompanied by pain and when the waves became regular the pain disappeared.

In studying these tracings one wonders whether the information obtained by the graphic method in other fields of investigation

Fig. 5. Action of atropine.

can assist us. The differences in amplitude of the waves obtained with the same size catheter and equal conditions in the recording apparatus in different patients suggest the possibility of these waves being some index of calycinal or pelvic output.

As S. W. Patterson and E. H. Starling (5) point out in regard to the heart, the output is equal to and determined by the inflow, and as long as arterial resistance is not raised the cardiac output may reach enormous proportions. If, however, the resistance to output is raised the venous pressure rises and the output may be appreciably affected. If the same set of conditions hold in regard to the kidney pelvis as in the heart, then we may establish the parallel in this wise. The outflow through the ureter corresponds to the outflow through the great arteries, the body of the pelvis corresponds to the ventricle, the calyces to the auricles and the urine flowing into the calyces from the collecting tubes corresponds to the venous inflow via the great veins. Now if the parallel still holds then "the output is equal to and is determined by the inflow" and as long as there is no resistance to output the pelvis can cope (within wide limits) with whatever amounts of urine are poured in. If, however, the resistance to the output is raised, then the pressure in the "ventricle" and calyces must rise till it reaches the secretion pressure of the urine when the flow must cease. We thus see what far reaching effects may be produced on the kidney locally and

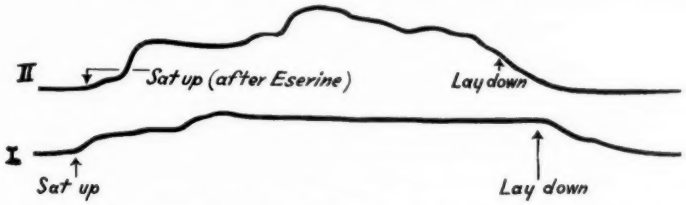


Fig. 6. Action of eserine. Effects of sitting up and lying down before and after injection. *I*, Before eserine. *II*, After eserine.

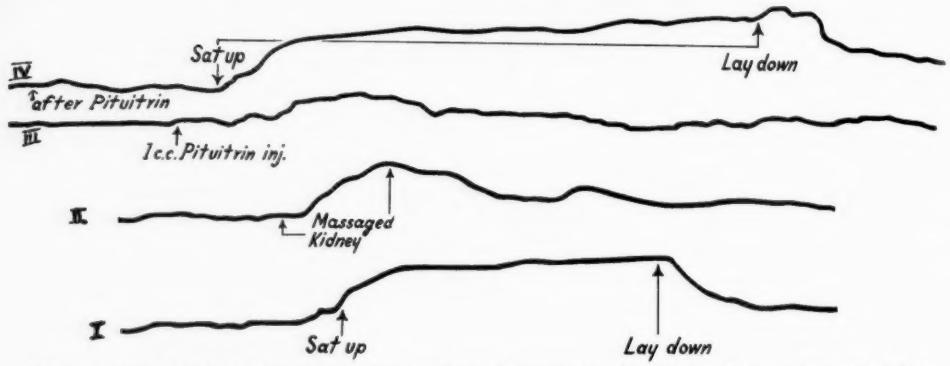


Fig. 7. Action of pituitrin. Note improvement in calycinal contractions in *III* after injecting pituitrin. *IV*, Improved response to sitting up after pituitrin.

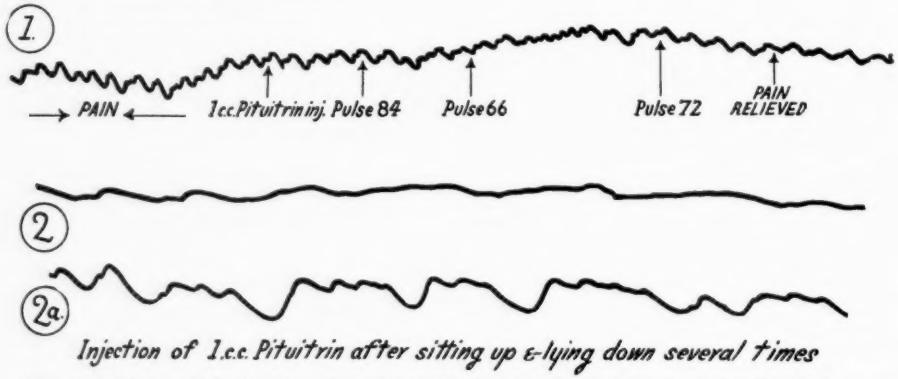


Fig. 8. Pelvic muscle dysfunction. Irregular contractions associated with pain. Pain relieved when contractions regular. In tracings *1* and *2* pain was associated with irregular contractions. Pain was relieved when contractions became regularized. *1*, by injection of pituitrin (Mrs. B., Fig 1, *I*). *2*, by injection of pituitrin after sitting up and lying down several times (Mrs. D., Fig. 1).

the system generally by conditions of spasm or physical obstruction or kinking in the ureter. Recognizing how frequently one sees spasm of the ureter with or without antiperistalsis in the neurotic (especially when some condition in the urine such as crystals of phosphate, oxalates, or uric acid, act as exciting causes of ureteric spasm), one wonders how often the vague backaches and headaches in these people may really be attributable to some actual disorganization of kidney function on the lines outlined above.

We do know that in many of these patients the outflow of urine from the ureter to the bladder is not regularly and evenly distributed over a unit of time. The complete interpretation of the tracings obtained must, however, be deferred until a larger series has been obtained.

There is another point suggested by these tracings which is borne out by pyeloscopy. In observing a pelvis comfortably filled with a watery solution of abrodil, 10 or even 20 contractions of the pelvis are often required to empty the pelvis. This suggests that the pelvis does not completely empty at each systole but retains a "maintenance filling" of urine, and as this is added to by the systole of the calyces, the contraction wave in the ventricle forces this excess out. The height of the waves, therefore, may be an indication not of the "pulse-pressure" in the pelvis but of the actual amount of fluid displaced from the pelvis at each systole.

We do know that in many cases of hydrophrosis, the pelvis may hold quite an mount of urine which runs away in a steady tream when the ureteric catheter is passed nto the pelvis, whereas in some cases of spasm f the pelvis practically no urine drips from he catheter on passage, the outflow being ntermittent from the outset. If the "maintenance filling" varies in amount according to arying physiological conditions of circulation, posture, rate of secretion, alterations in tone of the pelvis, spasm or obstruction of the ureter by pressure from adjacent structures, then it is easy to see how this variation may be reflected in alterations in amount or rate of kidney secretion, while at the same time a variation in the direction of over filling or complete emptying may determine some of those obscure kidney pains which are so difficult to define and elucidate and which yet often reduce the patient to a condition of semi-invalidism. A great deal more work is required on these lines before authoritative statements can be made on the subject but the results so far obtained by pyelometrical investigation of patients give one permanent records which can be compared with subsequent tracings and studied in connection with past or subsequent clinical findings. This preliminary investigation is also submitted in the hope that it may stimulate others with better facilities than the author possesses to carry out more extensive investigations on similar lines.

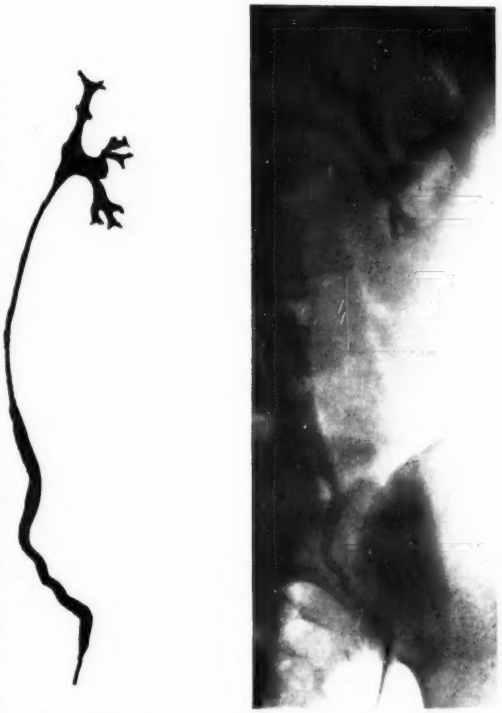


Fig. 9. Uretero-pyelogram. Mrs. McL. Spasm of kidney pelvis and upper part of ureter. The condition (and the pain) cleared up when quinine was given.

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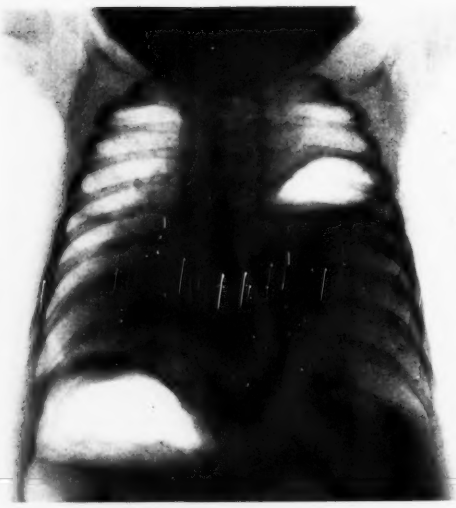


Fig. 1. Case 1. Balloon cyst. Roentgenogram showing fluid and small amount of air in cyst. These findings led to the erroneous diagnosis of hydropneumothorax.

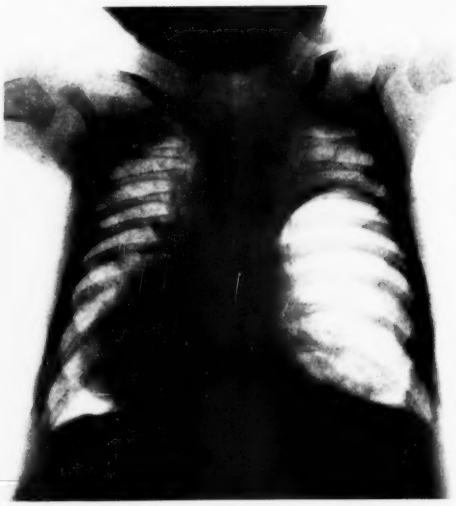


Fig. 2. Case 1. After spontaneous emptying of the fluid. Note the absence of collapsed lung at right hilum, but presence of normal lung markings at periphery which should help differentiate it from pneumothorax.

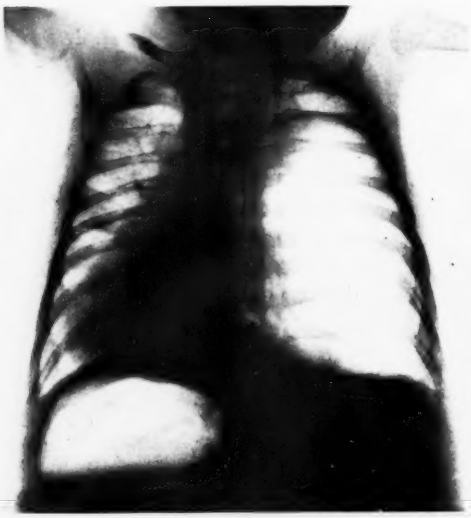


Fig. 3. Case 1. Roentgenogram made immediately after the withdrawal of 150 cubic centimeters of air. There is marked increase in the size of the cyst which is causing greater displacement of the surrounding structures.

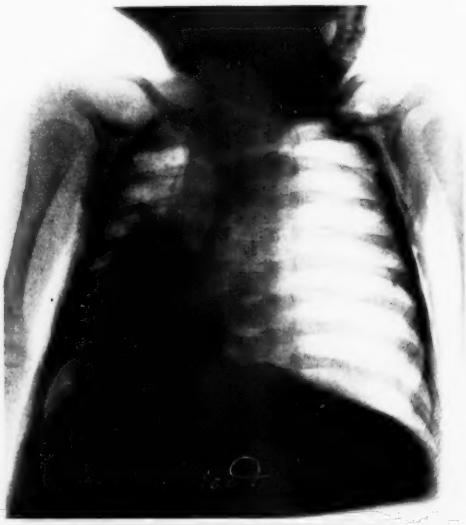


Fig. 4. Case 1. Postmortem roentgenogram. ill greater displacement of neighboring structures. te complete absence of lung markings on spine. The is marked decrease in density of the upper lobe, prol dy due to compensatory emphysema.

Large Pulmonary Air Cysts of Infancy.—William E. Anspach and Irving J. Wolman.

LARGE PULMONARY AIR CYSTS OF INFANCY

With Special Reference to Pathogenesis and Diagnosis[1]

WILLIAM E. ANSPACH, M.D., and IRVING J. WOLMAN, M.D., Chicago

APPROXIMATELY 150 cases of congenital lung cyst have been recorded in the American and European literature, but only a few of these were in infants, and in fewer still was the condition diagnosed and its course watched during life. In most instances the lesion was an accidental finding at necropsy.

In the 2 cases that we are about to report the diagnosis was made early and the patients were observed for a considerable time before death. The clinical and roentgen observations, taken together with the necropsy findings, suggest to us an explanation of the nature of air-containing lung cysts. This explanation is somewhat different from any of the many theories heretofore advanced as the result of necropsy study alone.

Case 1. Balloon cyst. M. K., a white male premature infant, had had a normal birth, but was kept in an incubator for 10 days because of his small weight of 3 pounds 6 ounces. He was breast fed and seemed to develop normally until 7 weeks of age, when his respirations gradually became difficult and rapid and a slight cough appeared. Physical examination by an attending pediatrician revealed a subnormal temperature and chest findings which were attributed to an atelectatic lung. There was no cyanosis or fever. The symptoms grew steadily worse, and he was admitted to the Children's Memorial Hospital on September 3, 1931, 2 weeks after the onset of symptoms. At this time, 9 weeks of age, he weighed 6½ pounds. There was dullness and absence of breath sounds on the right side of the chest, and the point of maximum cardiac impulse was found slightly to the left of the midsternum. Many râles were heard in the left lung. There were no evidences of congenital syphilis. The red count was 2,300,000, the hæmoglobin 55 per cent, and the white count 15,400, with a normal differential count. The diagnosis based on the physical findings was: congenital atelectasis of the right lung in a premature infant. An X-ray examination on the following day (Fig. 1) showed a dense shadow obliterating completely the lower half of the right lung field. Above this lay a dome-shaped pocket of free air, which had as its lower border a horizontal fluid level. Above this air pocket lay normal air containing lung tissue. These findings were interpreted as a right hydropneumothorax.

The infant took feedings well. There were frequent attacks of difficult breathing, with cough and slight cyanosis. Between paroxysms he was not cyanotic, but breathed rapidly. *He coughed up some viscous mucoid fluid on one occasion.* Another X-ray examination (Fig. 2) made 4 days later showed complete disappearance of the density from the right lung field; in its place was a large air containing cavity. A thoracentesis had not been done. In successive roentgenograms this cavity gradually increased in size, pressing the mediastinal structures to the left, and also the right leaf of the diaphragm downward. There was no evidence of a collapsed lung at the right of the spine. The apex of the right lung grew smaller and less dense as the amount of air increased in the cavity below. The diagnosis of pneumothorax was made, although one attending physician (Dr. E. T. McEnery), suggested the possibility of a lung cyst.

Labored respirations with cyanosis continued, and when 10 weeks old a thoracentesis needle was

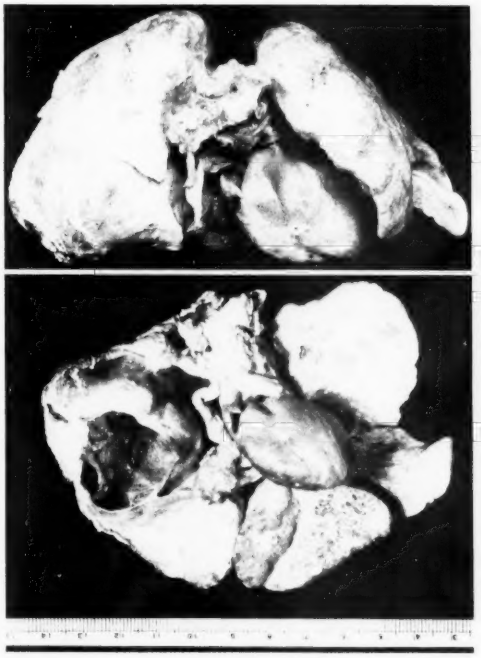


Fig. 5. Case 1. Anterior and diaphragmatic views of specimen (after fixation).

[1]From The Children's Memorial Hospital, and The Otho S. A. Sprague Memorial Institute Laboratory, Chicago.

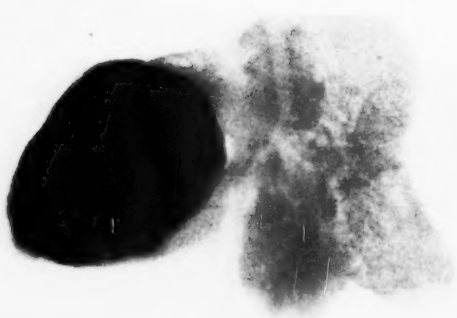


Fig. 6. Case 1. X-ray picture of specimen after cyst was filled with barium and gelatin.

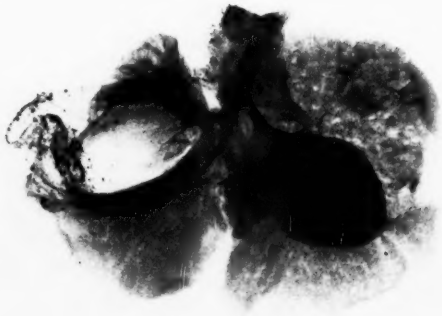


Fig. 7. Case 1. Injection of tracheobronchial tree showing bronchial distribution to region of cyst.

inserted to reduce the pressure. About 150 cubic centimeters of air was withdrawn, followed by relief of symptoms for but a few minutes. An X-ray (Fig. 3) taken 30 minutes later did not show the expected diminution, but instead an enlargement of the air containing space. Respiratory difficulty and cyanosis continued until death occurred 1 week later (age 11 weeks). Fever was not present at any time. Postmortem films (Fig. 4) showed the cavity to be larger and the mediastinal displacement even greater than in the films taken during life.

At necropsy, the body was small, poorly nourished, but well developed. It measured 45 centimeters in length and weighed $5\frac{1}{4}$ pounds. The thorax was well formed and symmetrical. No abnormalities were found except those within the chest. When an incision was made through the right costal cartilages, the sound of escaping air was heard.

A cyst-like air containing chamber was found within the middle lobe of the right lung. It occupied practically the whole right side of the thorax and displaced the mediastinal structures to the left. The left lung was compressed and pushed behind the heart. The heart was normal. Laterally the cyst wall was loosely bound to the right costal pleura. It could be freed by blunt dissection, although the thin and delicate wall ruptured in a few places during this process. The other lobes were free from cysts, had a normal architecture, and were apparently not

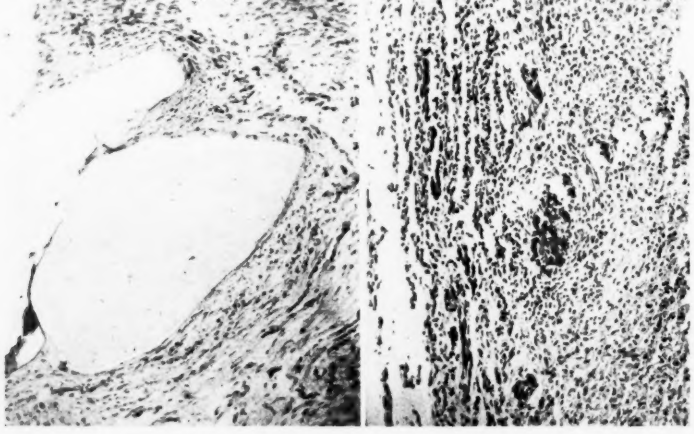


Fig. 8a, left. Case 1. Photomicrograph showing mesothelium lined fluid cysts found near the large air cyst. ×115.

Fig. 8b. Case 1. Photomicrograph of capsule of large air cyst, showing fibromuscular structure, absence of epithelial lining, and small bronchiole lying within wall. The adjacent alveoli are collapsed. ×135.

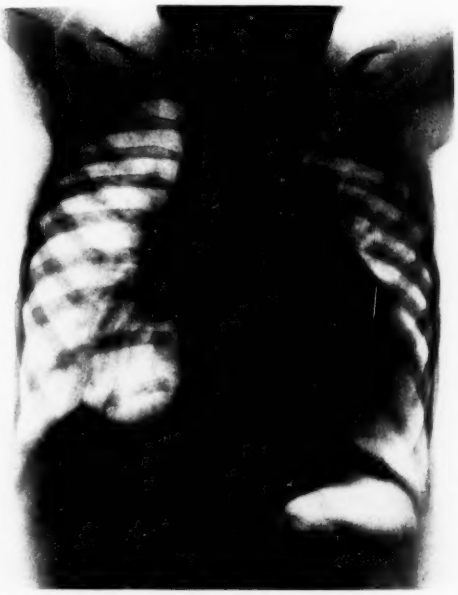


Fig. 9. Case 2. Stationary cyst. X-ray appearance when child was 15 months old. Note comparatively thin wall next to heart and diaphragm. A lateral view showed a corresponding relationship to the posterior wall.

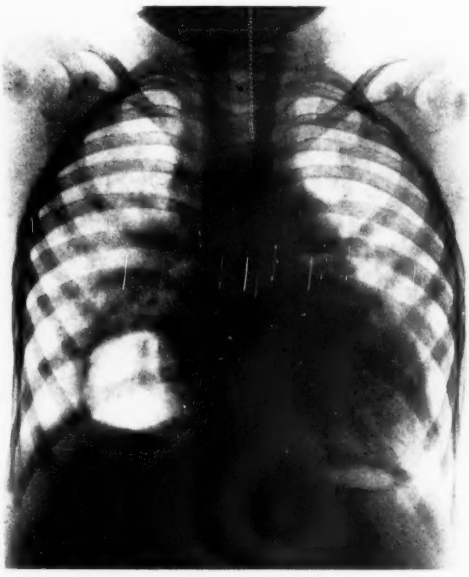


Fig. 10. Case 2. Unchanged appearance 10 months later. Several roentgenograms which were made in the interim failed to show any relative change in the size of the air pocket.

atelectatic. The upper and lower lobes adhered to the middle lobe, so that the fissures were recognizable only as a fine line, except on the posterior surface of the lung where they were well marked. The lower lobe lay posteriorly extending to the left of the spine. The small upper lobe sat on the cyst like a

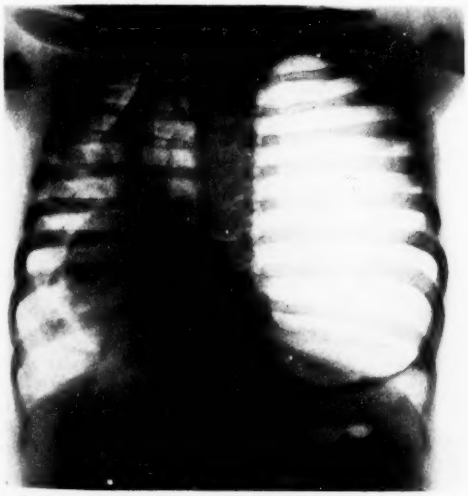


Fig. 11. Balloon cyst (Parmalee and Apfelbach). Note the cyst wall below and the absence of collapsed lung at the hilum.

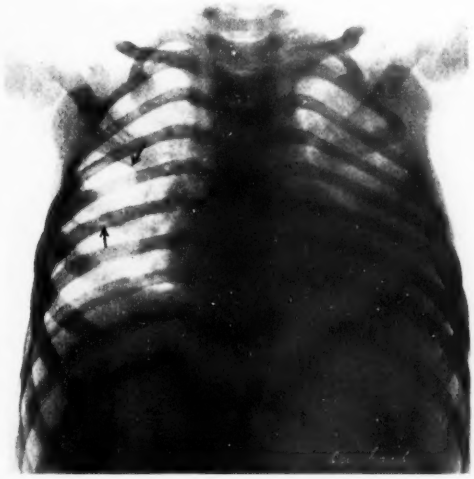


Fig. 12. Pneumothorax. Note oval area of decreased density in right axillary region simulating a cyst. Later this area disappeared.

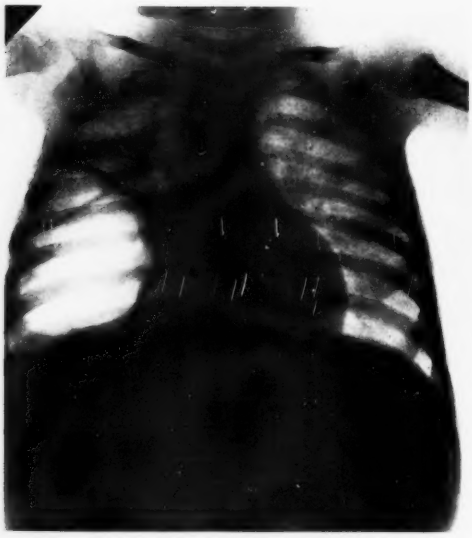


Fig. 13. Large "cyst-like" pneumothorax following pneumonia and empyema. Although there are changes in the upper lobe and hilum shadows, knowledge of the clinical course is necessary to differentiate it from a large solitary cyst.

cocked hat. Atelectatic middle lobe parenchyma was present on the posterior aspect of the cyst, and also on the mesial surface adjacent to the mediastinum. The cyst formed the lateral and anterior aspects of the middle lobe, and its inferior surface rested on the diaphragm. Its wall was thin, and was supported by contiguous parenchyma and the parietal pleura. The lining was smooth and white,

Fig. 14. Bulbous emphysema secondary to congenital atelectasis. Appearance easily confused with multiple air cysts. A comparison with other films of this case ruled out cysts because of the lack of uniform arrangement of film densities at different examinations.

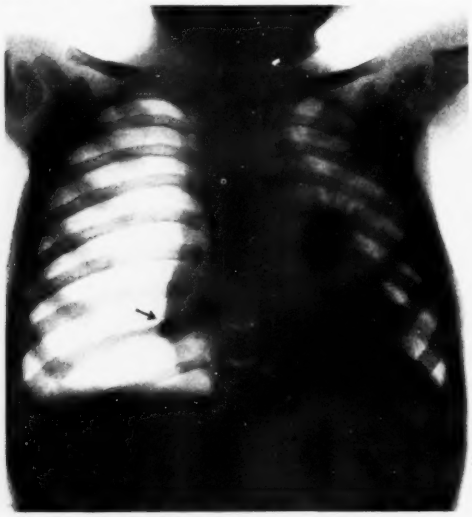


Fig. 15. Massive positive pressure pneumothorax following empyema. Arrow shows collapsed lobes which have retracted from the diaphragm. This point aids in the differentiation from lung cyst.

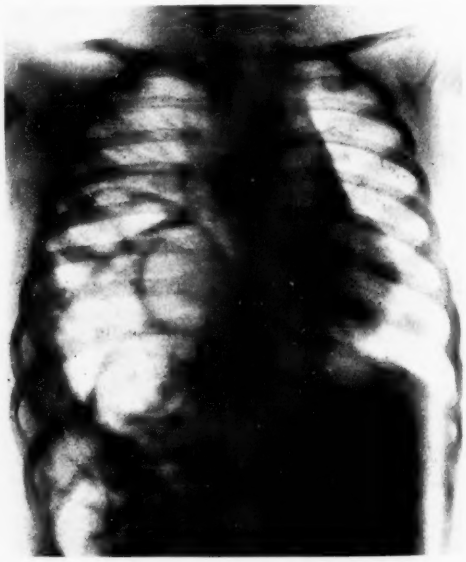


Fig. 16. Eventration or herniation of the diaphragm, resembling multiple lung cysts, may be diagnosed by the appearance of opaque shadows in this portion of the lung field following a barium meal.

and a fine deposit of white granular matter clung to the lower portion. At the hilum, there were a few dimples and puckerings, and when the lungs were insufflated under water, a stream of bubbles came from this region.

The right main bronchus divided into two branches. The inferior branch extended into the lower lobe; the superior divided into a large trunk which ran to the upper lobe, and a short trunk which supplied the middle lobe (Fig. 5).

Microscopic examination: The alveoli of the middle lobe were partially collapsed, but otherwise normal. In two different regions, atelectasis was complete, and here groups of microscopic cystic chambers ramified through the parenchyma among the alveoli. These cavities were of different sizes and outlines, some being circular, others long, tortuous, and branching. Some chambers were dilated and filled with a clear albuminous coagulum, their inner surfaces being outlined by flat cells of mesothelial character. The walls consisted of a thick layer of compact laminated fibrous tissue. Tiny fluid filled cysts, identical in structure, were situated in the wall of these larger ones (Fig. 8a). A few chambers were collapsed, with inflammatory mononuclear cells and multinucleated giant cells within their lumin and walls. These small cystic chambers, microscopic in size, were situated in the neighborhood of the large air containing cyst (which had a similar structure). The wall of the latter was made up of laminated cellular fibrous tissue containing numerous scattered smooth muscle cells (Fig. 8b). Occasional clumps of wandering inflammatory cells adhered to the inner surface. Its outer margin was somewhat indefinite and blended into the stroma of the surrounding atelectatic alveoli. In some sections, the wall of the cyst was thin, consisting of only a single layer of connective tissue supported by collapsed alveoli; nowhere, however, was the capsule completely absent. No elastic fibers could be stained within the walls of the cysts, or in any part of the lung tissue except the medial coat of the pulmonary arteries. No epithelial cells, secretory glands, or prominent blood vessels could be found.

In the neighborhood of the middle lobe bronchus, a small patent bronchiole (Fig. 7) lined with columnar epithelium lay within the cyst wall. It seems highly probable that this was the channel of communication between the cyst cavity and the bronchial tree, although no direct communication was found in a series of sections.

The following anatomical diagnosis was made: prematurity; congenital lymphangiectatic cystic formation in right middle lobe of lung; communication between a large chamber and a terminal bronchiole, with the formation of an air containing thin walled cyst; displacement of heart and mediastinum to left; compression of left lung; malnutrition.

PATHOGENESIS

Congenital pulmonary cysts are found in individuals of all ages and in a variety of forms. They are usually multiple, and may be scattered, grouped, or confluent. Usually they are restricted to one lobe; occasionally the distribution is through both lungs. They may contain mucoid fluid, desquamated matter, air, or pus. A small percentage appear to be lymphangiomatous formations. Other cysts, which arise from the mediastinum, are derived from ectopic islets of the primitive gut, and possess a lining of œsophageal or gastric mucosa. The large majority of the cysts, however, possess a lining of cuboidal epithelium supported by fibrous tissue, smooth muscle, and cartilage, and seem to be bronchiogenic in character. For the pathogenesis of this last group, a variety of theories has been proposed, including congenital bronchiectasis (11), excessive growth of interstitial fibrous tissue (1; 32), defective energy of growth (18), underdevelopment of alveoli, counterbalanced by widening of the bronchi (6; 24), and congenital atelectasis (10; 12). Congenital syphilis (28), fetal pleural adhesions (25), neoplastic processes (20), and bronchopneumonia (4) have also been suggested. All such speculations as to origin have been based almost entirely on the morphological evidence of necropsy findings. In most instances, postnatal changes caused by respiratory action, rupture of the cyst, or the presence of infection have confused and distorted the primary pathological picture. The reader is referred to a summary of 108 cases by Koontz (17), 1925, and to a more recent critical discussion of the theories of origin by Mueller (23), 1928.

There can be little doubt that the cysts found early in infancy are true congenital malformations, arising from several different sources in embryonic life. However, once a large cystic cavity has been formed, its behavior should be determined largely by mechanical and accidental influences, such as capsular strength, proximity of adjacent air passages, plasticity of the surrounding lung tissue, and the presence or absence of complicating respiratory infections, rather than by its embryogenesis or histology of its lining.

The consensus of investigators has been that large air cavities are preformed but col-

lapse at birth and distend at the first inspiration, or else that they develop from small congenital bronchiectatic dilatations, which enlarge in postnatal life as the result of stenosis of their orifices. However, a third possibility suggests itself: the large air cyst may have been primarily a large fluid filled sac which evacuated itself spontaneously by rupture into a bronchus, and became filled with air.

Just such an origin was manifested by our air containing cyst (Case 1) which originally had been a large fluid filled chamber within a congenital cystic malformation of the lung. While under observation its fluid content disappeared, presumably following rupture into a bronchiole. A small quantity of mucoid material was coughed up and the remainder was apparently swallowed. The emptying cavity, instead of collapsing, filled with air; it then proceeded to dilate and "balloon out" as the result of valve-like behavior of its bronchiolar opening, and eventually produced respiratory difficulty and death. These changes were followed roentgenologically, and verified at necropsy. So far as we have been able to determine, this is the only instance where such a series of events has been followed clinically.

On histological examination the cystic formation appeared as a lymphangioma ramifying through the alveolar septa. Although the large majority of lung cysts reported have resembled epithelium-lined bronchioles, in Virchow's case, and in those of Meyer and Kessler, as restudied by Klebs, similar mesothelium-lined cysts, considered lymphangiectatic, were scattered through the interstitial pulmonary framework.

Lung cysts are so rarely diagnosed during life that not much is known about their clinical behavior. When a large cyst is found in an adult, one cannot say whether it had been present in essentially the same form since infancy, or had recently developed, or had changed its form and size within the past few years. The number of cases reported with satisfactory clinical studies is very small. The recent articles of Miller and Eloesser are doing much to arouse interest in the subject in this country.

We have found reports of 5 lung cysts which, at the time of discovery, were large and air containing, and which in their clinical behavior were identical with our case in its later stages. These occurred in infants in whom symptoms of respiratory distress had begun some weeks after birth. All showed extreme distention or steady increase in size. The cysts that were aspirated promptly refilled with air. Those examined at necropsy were found to possess a narrow communication with some bronchiole, which usually entered by a tortuous or oblique route. None of the patients survived 18 months of age. A brief review of each case follows:

An infant girl, having a large, solitary, air containing, expansile cyst, was reported by Parmalee and Apfelbach. She had been seen at The Children's Memorial Hospital when 11 weeks of age because of frequent attacks of dyspnœa and cyanosis, and presented clinically the signs of pneumothorax. Aspiration of air was followed by collapse, necessitating the use of artificial respiration to maintain life. From that time on, the child went along with moderate symptoms of respiratory distress, until she succumbed to a complicating bronchopneumonia at 17 months of age. Necropsy revealed an enormous epithelium-lined cyst with a bronchiole entering it by a devious course through a network of identical microscopic chambers lying within the wall of the main cyst. The lung covered only one-half of the cyst surface.

Altmann observed a structurally similar formation in the lung of a female infant who died at the age of 2½ months with a diagnosis of pertussis bronchopneumonia. The right lower lobe contained a gas filled cyst, which, after fixation, measured 7 by 5.5 by 4.5 centimeters. Half of its upper surface lay immediately below the parietal pleura; the remainder was in intimate association with the lung parenchyma. It had a thin wall with a smooth, glistening inner aspect, and two semi-circular partitions on the posterior surface. A bronchiole, the size of a small bristle communicated with the cyst.

Miller, in 1926, described a large air containing cyst, as demonstrated by roentgenological and clinical signs, in a child 5 weeks old. There were severe attacks of dyspnœa lasting from 15 to 20 minutes. At first the condition was thought to be a pneumothorax on the right side, displacing the mediastinum and heart to the left. Repeated thoracocenteses released air under pressure, and gave temporary relief from the respiratory embarrassment. Later, a small rubber tube fitted with a one way valve which allowed the escape but prevented the aspiration of air, was inserted into the cavity. Marked improvement occurred. After the air containing pocket had decreased greatly in size, the

tube was removed; 2 weeks later the cyst was found to have regained its original volume. The child died at the age of 5 months, apparently from asphyxia. No necropsy was performed.

Burghard (1926) described a large air distended cystic cavity in the left lung of a 2 months old infant, who died of a terminal bronchopneumonia. Dyspnœa had been present since 2 weeks of age. The cyst was found within the parenchyma of the lung, which itself was emphysematous. The opposite lung was a little compressed, and the mediastinum displaced to the right. The cavity communicated with the bronchial tree through a tiny bronchiole. Its wall was thin; the microscopic structure was not reported.

Huenermann and Sievers (1930) describe a multiloculated cystic formation, or "honeycomb lung," which filled the left chest of a 2 weeks old infant, causing dextroversio cordis and compression of the right lung. This was air containing when the infant was first seen; it rapidly increased in size, and produced symptoms of cyanosis and dyspnœa. Thoracentesis removed air under pressure but gave no relief of symptoms. Death occurred at 3 weeks of age. The postmortem X-ray film showed a left pneumothorax, with the cystic left lung partially collapsed and clearly outlined. Necropsy demonstrated multiple, distended, air containing chambers within the left upper lobe. Several entering bronchioles were present.

A suggestion as to pathogenesis is ventured in the first three of the above reports, and each author assumes that the large cystic chamber began as a small air containing bronchiectasis which dilated in postfetal life. Inasmuch as in all but one, a large portion of the wall was situated subpleurally, it would follow that, in expanding, the cyst must have torn its way peripherally through enveloping lung parenchyma within the short space of a few weeks. One would expect to find, therefore, as a consequence of the quick gigantic increase in size, a greatly stretched, thin walled capsule and a flattened lining, with some areas of rupture. Instead, however, these cysts characteristically had the opposite structure, with well developed columnar epithelial lining and thick fibromuscular capsules.

In our own case with a wall thinned in places, this change was due to secondary ballooning with air after the fluid contents had been discharged.

Because of the similarity in gross appearance, age incidence, and clinical behavior of the above air cysts to the later stages in our case, it seems probable that they all had a similar beginning, i.e., from the rupture of a fluid containing cyst. Their well developed walls are consistent with this interpretation, as is also the presence, in each, of an entering bronchiole. Rupture and evacuation must then have occurred soon after birth.

Swanson, Platou, and Sadler in 1928 reported a solitary fluid containing cyst noted in an infant 7 weeks of age. There were frequent attacks of cyanosis and dyspnœa, and the right side of the chest showed impaired resonance and suppression of breath sounds. X-ray examinations revealed a dense opaque area throughout the whole right side of the thorax, with some areas of decreased density near the base. The heart and mediastinum were displaced to the left. After it was tapped, the cyst refilled rapidly with prompt recurrence of symptoms. An open fistula was made surgically when the child was 3 months old, and the cavity was irrigated repeatedly. In 2 months it decreased in volume from approximately 200 cubic centimeters to 8 cubic centimeters, as measured by sodium iodide injections. There was no evidence of an open communication with a bronchus. The child died following a bronchoscopic examination. Cells of glandular tissue were found in the wall of the contracted cyst at necropsy.

This large fluid cyst occurred in an infant whose age was comparable with that of the cases of air cysts discussed. If rupture into a bronchus had occurred, we believe it would have shown the X-ray appearance and expansile behavior of the air cysts already described. Its clinical manifestations resembled closely that of our own case when first observed.

Several reports have been made of cysts structurally like those in the case of Huenermann and Sievers, but containing fluid instead of air. These were found in stillborn fetuses or in infants living only a few hours. Wolman described a dilated fluid filled bronchiogenic cystic structure in the lungs of a 6 months stillborn fetus. Pappenheimer reported an identical cyst in an 8 months premature infant who lived only 3 hours. No communication with the bronchial tree could be demonstrated in either case. In Kessler's 6 months old fetus, cystic fluid filled lymphangiectatic chambers ramified through the pulmonary framework. Grawitz also described a fluid filled cyst in the lung of a newborn. Obviously postnatal factors can be ruled out in these instances. It seems likely that many of the

cases reported as congenital bronchiectasis originated as similar cysts in fetal life.

It is necessary that all air containing cysts possess an outlet into the bronchial tree, patent at intervals if not continually, since otherwise the contained air would be absorbed in the course of time. In the group of large air cysts described, all maintained their large volume, and some increased in size, which indicated that air entered more rapidly than it was absorbed. It seems probable that the communicating bronchiole, entering the cyst cavity by an angular tortuous course, acted as a valve allowing entrance but preventing outflow of air. At each expiration, air pressure within the cyst became raised temporarily above the external intrathoracic pressure, with a resultant expansion and gradual stretching of the wall, until the maximum size permitted by structural conditions of the lung and mediastinum was attained. As the cyst expanded, labored breathing and cyanosis resulted, just as would occur in massive pneumothorax, and death ensued from asphyxia unless the process ceased spontaneously or was interrupted by surgical interference.

It is easy to understand why these expanding cysts are not encountered in older children and in adults. In premature and young infants, all tissues (37) including the pulmonary parenchyma, are relatively weak, friable, and poorly resistant to the strains of tension and other trauma. In our first patient, a premature infant who was 11 weeks old at death, the pulmonary elastic fibers which normally appear in the first or second month postpartum (19) had not yet developed.

If there is no valve action at the communicating bronchiole, or if the location of the cyst is such that neighboring structures support it, or if a chronic infection has provided support by causing a deposition of fibrous tissue, the cyst may remain constant in size. The following case seems to support this view.

CASE 2. Non-expansile cyst. A premature female child was observed for 10 months at The Children's Memorial Hospital, during which period she had frequent bouts of fever, with cough and dyspnœa, sufficient to require admittance to the wards on four occasions. She was constantly undernourished, her greatest weight being 12 pounds 8 ounces. No physical signs of a cavity within the lung were elicited; the most constant chest findings were impaired resonance and higher pitched breathing in the right lower lobe behind. Frequent roentgenological examinations, during each period of hospital care, showed a constant oval area of decreased density in the right lung at the cardiohepatic angle. The lateral border of the cavity was dense, and the hilum markings above it were prominent presumably because of superimposed infection. Death from bronchopneumonia occurred at 25 months of age. Necropsy permission was not obtained. The diagnosis was: chronic bronchitis and bronchopneumonia, congenital cyst of lung, congenital heart defect, bilateral cataract, malnutrition. We believe that the diagnosis of a congenital cyst, rather than a localized pneumothorax, is favored by the contour of the air pocket, its location and failure to absorb, and the associated presence of other anomalies. Steinmeyer (31) and Eloesser (9) have described somewhat similar cases.

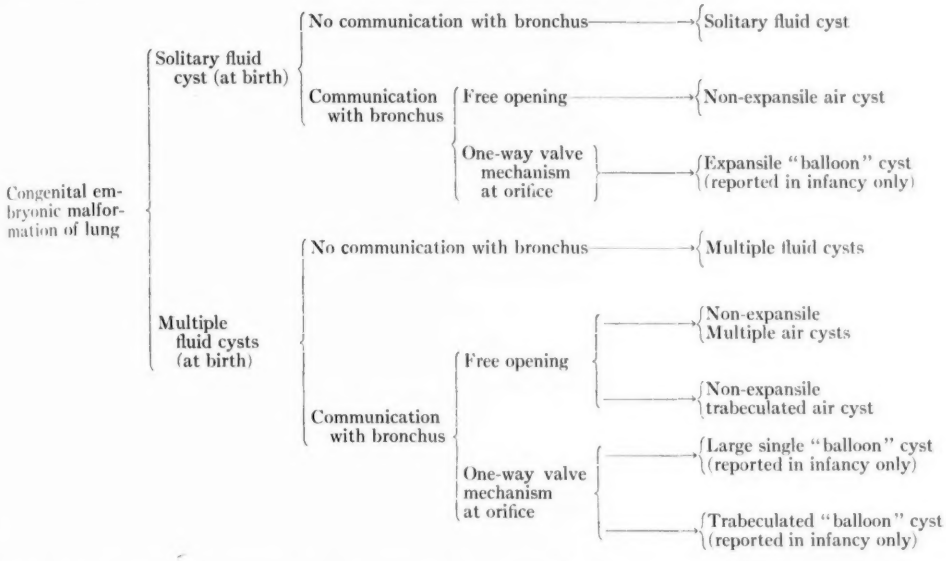
Based upon the above observations and discussion, we venture the classification of lung cysts as shown in Table I.

DIAGNOSIS

Large cysts occurring in the lungs of infants produce first an increase in the respiratory rate and later cyanosis. If the cysts contain fluid there may be local dullness and absence of breath sounds, but if they are filled with air there is hyperresonance and the breath sounds are faint or high pitched. If marked displacement of the heart and mediastinum occurs, percussion dullness may appear over the normal lung as it becomes compressed. Large cysts may produce dyspnœa, difficulty in swallowing, or cough, and in extreme cases the chest may bulge. Small cysts may produce no symptoms at all or only those due to superimposed infection.

There appear to be no pathognomonic roentgenological characteristics of a fluid containing cyst; but a large dense shadow surrounded by normal appearing lung tissue in an otherwise quite healthy infant, should arouse suspicion of that condition. Contralateral displacement of the medistinum is usually not, by itself, a dependable sign. In infants, an erroneous diagnosis of atelectasis is most likely to be made, as occurred in the early stages of our Case 1. Aspiration of viscid fluid may be necessary to differentiate between

TABLE I.—SUGGESTED CLASSIFICATION OF CONGENITAL LUNG CYSTS ON THE BASIS OF POSTNATAL BEHAVIOR


Congenital embryonic malformation of lung
Solitary fluid cyst (at birth)
No communication with bronchus
Solitary fluid cyst
Communication with bronchus
Free opening
Non-expansile air cyst
One-way valve mechanism at orifice
Expansile "balloon" cyst (reported in infancy only)
Multiple fluid cysts (at birth)
No communication with bronchus
Multiple fluid cysts
Communication with bronchus
Free opening
Non-expansile Multiple air cysts
Non-expansile trabeculated air cyst
One-way valve mechanism at orifice
Large single "balloon" cyst (reported in infancy only)
Trabeculated "balloon" cyst (reported in infancy only)

a fluid filled cyst and encapsulated fluid from other causes.

Upon the roentgenological findings chiefly does the differentiation between positive pressure pneumothorax and "balloon" air cyst depend. In the latter, the air containing cavity lies *within the lung* and enlarges as the gradual addition of trapped air, by exerting a uniform outward pressure, stretches the cyst wall and displaces the surrounding lung tissue around it in all directions. Consequently the lung tissue can be recognized upon the film as normal or varied densities at the apex, the costophrenic, and the cardiohepatic angles. The shadows of hilum structures on the mesial side of the lung field soon fade, partly because of their migration about the surface of the cyst, but principally because of the early displacement of the easily movable mediastinal boundary of the lung contralaterally. In massive pneumothorax, on the other hand, the air lies in the pleural cavity separating the normal contact of the visceral and parietal pleuræ, and exerting pressure from *without the lung* upon its entire pleural surface. This pressure produces collapse of the whole lung with displacement of the mediastinal structures to the opposite side. The lung parenchyma at the hilum is not thinned out nor are there the shadows of tissue at the apex and angles. A readily noticeable differentiating point is the retracted collapsed lower lobe in massive pneumothorax (Fig. 15). Visualization of a dense curved line, which assists in making a diagnosis of a cyst in the presence of other evidence, must not be depended upon as a pathognomonic sign when occurring by itself, since adhesive bands, as in pneumothorax following empyema, may produce a somewhat similar appearance. A trabeculated cystic cavity may show as a network of thin densities on the film and may be confused with multiple bands of pleural adhesions. Here the history of a previous pneumonia or empyema supports the diagnosis of pneumothorax. It is significant that our Case 1 was called pneumothorax by all the members of the staff except one, who was familiar with the roentgenograms of a previous case of balloon cyst, and noted the resemblance.

Massive pneumothorax, complicating a solitary cyst, aids rather than confuses the diagnosis, if the pleural air happens to be

distributed so as to outline the contour of the collapsed cystic lobe. This point is beautifully demonstrated in the illustrations accompanying the report of Huenermann and Sievers.

Smaller air cysts are recognizable as rounded areas of decreased density with a smooth linear outline. When conditions permit, radiopaque oil dropped into the bronchus may fill the cavity or may make its contour more clearly evident by filling the adjacent bronchial tree. The differentiation between a small air cyst and a localized pneumothorax (Figs. 12 and 13) may be difficult or even impossible at a single roentgen examination. Repeated observations, however, will usually show "fixity" in the case of a cyst and definite lability in a pneumothorax.

Bullous emphysema (Fig. 14) often appears as multiple air containing areas of decreased density upon the X-ray film. In infants these are frequently secondary to irregular areas of atelectasis which show as increased densities. Successive examinations will usually demonstrate that the air containing spaces and the dense atelectatic portions fluctuate somewhat in density and relative size. There is also, of course, absence of a dense linear "cyst" wall.

True diaphragmatic hernia or eventration of the diaphragm (Fig. 16) with gas or fluid in the thoracic portion of the intestine or stomach can simulate roentgenologically, as well as clinically, solitary or multiple air or fluid containing cysts. Fluoroscopic examination, following the administration of oral barium, will demonstrate the misplaced stomach in the thorax, and subsequent X-ray films will outline the cyst-like loops of the herniated intestine.

Duken and Vollmer have each described a case of "pneumatocele" following pneumonia, in which a large air containing oval was found in the lung. Since these completely disappeared following a single aspiration, we believe that a localized pneumothorax could better explain the findings. In our experience and that of Bigler (2), subpleural blebs do not attain a large size, and we have never been able to demonstrate them on the postmortem X-ray films taken before the necropsy which reveals their presence.

Stein's (29) case reported as congenital pneumothorax was 1 week old when first observed and is 2½ years old now (30). The published films demonstrate a sharply outlined air pocket with pneumatic lung at the costophrenic angle, a condition that is characteristic of large solitary cysts. We have, moreover, been unable to find a report of any case of congenital pneumothorax proved by necropsy.

A cyst filled with fluid usually presents a poorly defined margin, scarcely to be confused with the sharp borders of chondroma (13), ganglioneuroma (3), or echinococcus cyst.

TREATMENT

A thoracentesis was done in 4 cases of balloon cyst that were studied during life. Two were temporarily relieved (our Case 1 and Miller's patient). Another (Parmalee and Apfelbach's) collapsed during the procedure and was revived by artificial respiration; the fourth (Huenermann and Siever's) developed a pneumothorax which hastened the exitus. A drainage tube, with a valve allowing only the outlet of air, gave effective relief, for a few days, to Miller's patient. A large fluid cyst in a small child (Swanson, Platou, and Sadler) was drained and became greatly reduced in size. While surgical removal of lung cysts has been successfully accomplished in adults, it has not been attempted in infants. It is hoped that through a greater knowledge of the pathogenesis and behavior of congenital lung cysts, recognition during life will occur more often, and that a satisfactory treatment will eventually be devised to prevent the present high mortality in infants and young children.

SUMMARY

Two cases of lung cyst observed in infants are described. One of the cysts originated as a large lymphangiectatic fluid filled chamber, which evacuated spontaneously and then "ballooned out" with air, producing a fatal outcome. The other, which was not verified by necropsy, showed a constant X-ray appearance over a long period.

Fluid cysts in infants, which are usually mistaken for atelectasis, do not have a char-

acteristic roentgenological appearance, but air containing lung tissue about an area of increased density should arouse suspicion of the presence of a cyst.

The diagnosis of balloon cysts depends upon successive X-ray and clinical studies and upon an understanding of the late stages of pathogenesis. Usually an erroneous diagnosis of pneumothorax has been made. The main roentgenological diagnostic points of a balloon cyst are the presence of lung tissue at the apex and angles and its absence at the usual hilum region. A collapsed retracted lung shadow, as in simple massive pneumothorax, is not seen on the film.

Small air cysts, which cannot be differentiated from other air pockets, such as localized pneumothorax, at a single examination will maintain a more or less constant appearance, while the others will show changes and later disappear.

Based upon a study of reported cases and of their own observation, the authors believe that congenital air cysts of the lung are fluid containing at birth, and that their postnatal behavior depends principally on mechanical factors. A classification of congenital lung cysts is suggested.

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STUDIES IN PHYSIOLOGICAL AND PATHOLOGICAL UTERINE MUSCULATURE AT TERM

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UTERINE musculature at term, presents a most interesting field for investigation, yet there is very little to be found on the subject in medical literature. In order to appreciate the difference in the structure of normal and pathological uterine musculature, such staining of the sections was utilized as to color the muscle fibers deep red and the connective tissue moderately deep blue. The staining method used for the preparation of the sections here presented is a modification of the azan method as described in Romeis' *Tashenbuch der mikroskopischen Technik* according to Heidenhain and Mallory, but with shortening of the time of the staining with a marked increase in the tissue contrast. The following method was used:

The sections were prepared in paraffin. The slides were then deparaffinized by passing them through xyol, alcohol and water; then into azocarmin[1] (muscle stain), and for 45 to 60 minutes kept in the incubator at 55 to 60 degrees centigrade; removed from incubator and kept at room temperature for 5 to 10 minutes. (If the stain has been previously heated, the slides should be kept in the stain for only 15 minutes.) Following this, the sections were differentiated in alcohol aniline dye (1 cubic centimeter aniline oil to 1000 cubic centimeters of 90 per cent alcohol) for ½ to 1 minute; were stood in acetic acid alcohol solution (1 per cent acetic acid made in 96 per cent alcohol) for 3 to 4 minutes, and were then placed directly into 5 per cent aqueous phosphotungstic acid for 45 minutes and again washed with distilled water. The connective tissue was stained next by placing the slides in aniline blue orange[2] acetic acid for 45 minutes and again washed with distilled water, following which they were differentiated in 96 per cent alcohol for a few minutes, in absolute alcohol, xyol, and then mounted.

Careful studies in the arrangements of muscle fibers have been made by William Hunter in England; Madame Boivin, Deville and Helie in France; Roederer, Luschka, Henle, Hoffman, Bayer, Hofmeier and others in Germany, but unfortunately their investigations have not led to uniform results.

The myometrium, a muscular coat, although composed of bundles of involuntary muscle arranged with little individual regularity, may be considered as having an innermost circular layer, a thick middle layer, in which the bundles possess a general tendency toward figure-of-eight formation in a most irregular fashion of network of interlacing fibers, and a thin imperfect outer layer in which their course is for the most part longitudinal. However, in the uterus there is really no uniform arrangement in layers such as circular or longitudinal as may be found in other organs. The interlacing and crossing muscle bundle in the thick middle layer is, according to Henle and Luschka, the main layer of the uterus and is a dense network of muscle fibers. This thick middle layer is distinguished by the intermuscular connective tissue being vascularized in all directions by blood vessels, and hence is known as the stratum vascular. This muscle layer is confined to the uterus except below where it becomes continuous with the muscle of the vaginal wall. The longitudinal muscle bundles of feeble outer layer, which is present only over the fundus and body, are continued beyond the uterus on to the tubes and into the broad, round, ovarian, and uterosacral ligaments.

The individual muscle cells are unstriated and of various shapes, usually elongated spindle shaped, or as rarely seen, short and

[1] Azocarmin B—0.25 per cent to 1 per cent plus 1 cubic centimeter glacial acetic acid and add up to 100 cubic centimeters water, or azocarmin G—1 per cent boiled for 15 minutes plus 1 cubic centimeter glacial acetic acid and filter warm.

[2] Aniline blue orange acetic acid—aniline blue, 0.5 grams; gold orange 2.0 grams; water 100 cubic centimeters; glacial acetic acid 8.00 cubic centimeters—heat to boiling, cool and filter. To use dilute 1 and 2 with water.

Fig. 1. Uterus, cæsarean section. Azan stain.

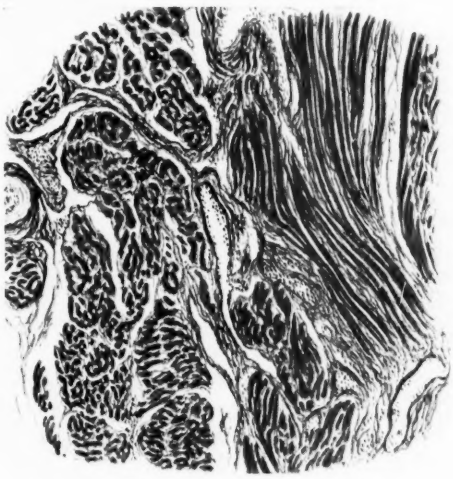

Fig. 2. Uterus, cæsarean section. Azan stain.

broad. In a few instances, striated muscle fibers have been found in the uterus postpartum near the placental site. Their length varies from 0.040 to 0.060 millimeters. On transverse sections the cells usually appear round, ovoid or polygonal, somewhat like a red cell but with the less defined outline and in many cells the nucleus is not on the plane section. The nucleus in the long diameter of the cell is ordinarily rodlike, but if fixed during the contraction is sickle or half moon shaped.

During pregnancy the enlargement of the uterus is not symmetrical, but is marked in the fundal region. This can be readily appreciated by observing the relative position of the insertions of the fallopian tubes and the ovarian ligaments, which in the early months of pregnancy are almost on a level with the fundus; and in the latter months their attachments are found to point slightly above the middle of the organ. The increase in size and thickness of the walls of the uterus are brought about by combined hyperplasia and hypertrophy or increase in number of the individual muscle fibers. The position of the placenta also exerts a determining influence upon the extent of the hypertrophy, the portion of the uterus to which it is attached enlarging more rapidly than elsewhere, as is clearly shown by the position of the uterine ends of the round ligaments, which are close together when the placenta is inserted upon the posterior and far apart when it is upon the anterior wall. Postpartum, the uterus is enlarged to a varying degree, even if involution is complete. On section the musculature appears coarse and the blood vessels stand out

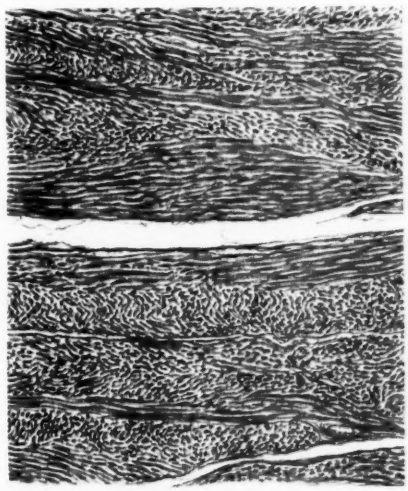

Fig. 3. Uterus, cæsarean section. Postmortem. No labor.

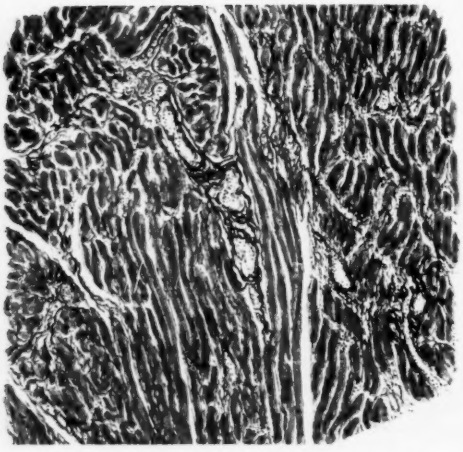

Fig. 4. Normal uterus postmortem. Azan stain.

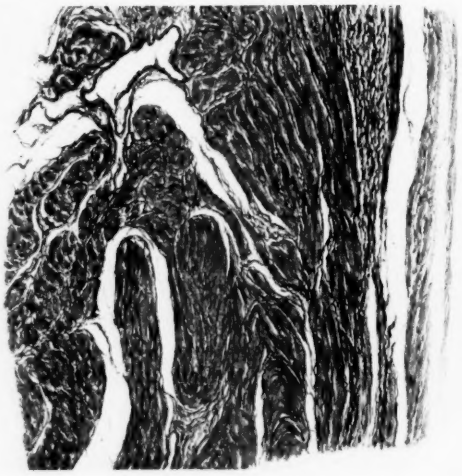

Fig. 5. Placenta prævia. Uterus, cæsarean section. Azan stain.

above the surface. Microscopically there may be a preponderance of connective tissue and there is usually some lack of uniformity, the involution being more advanced in some parts than in others.

In the uteri studied, the structure of the fibers was compared as to size, shape, and staining ability, and the amount of connective tissue was carefully noted. The low power magnification only is demonstrated. The fibers were measured as to the number per millimeter and at least ten fields were counted on each preparation and the average taken to determine the width of the fibers. The length could not be calculated as accurately.

Figures 1 and 2 are sections from uteri removed after cæsarean sections. The muscle fibers are heavy, very long and deep staining. There is very little intrafasicular connective tissue and a slightly greater amount of interfasicular connective tissue with an average of 22.4 to 30.5 fibers per millimeter respectively in the width.

Figure 3 is a section from a uterus. A cæsarean section postmortem which was performed to get a living baby from a woman at term who was killed by a fall. She had had no labor pains. Here too the fibers appear to be very long and deep staining, but thin. The intrafasicular and interfasicular connective tissue were both scant. The average width of the fibers is 36.7 fibers per millimeter.

Figure 4 is a normal postpartum uterus removed after death of the mother. The muscle fibers are very long and heavy, as well as deeply staining. The transversely cut fibers are also very thick and there is barely enough intrafasicular connective tissue to be able to distinguish the individual fibers and there is a scant amount of interfasicular connective tissue. The average width of the fibers in this section is 25.4 fibers per millimeter. Figure 5 is a section from a uterus of a case of placenta prævia. Here the musculature appears like that of the normal uteri removed after a cæsarean section, and there is similar paucity of both intrafasicular and interfasicular connective tissue. The average width is 23.7 fibers per millimeter.

Figure 6 is that of a section of a uterus from a case of placenta acreta. The longitudinal fibers appear to be shorter and the transversely cut fibers smaller. There is not an equal staining throughout, many parts of fibers being only lightly stained. The average number of fibers per millimeter is 27.6 in their width. However, the number is proportionately greater because of a fair amount of intrafasicular connective tissue, with only a slight increase in interfasicular over the normal.

Figures 7 and 8 are two sections taken from the same organ, an atonic uterus, labo[ra]tory

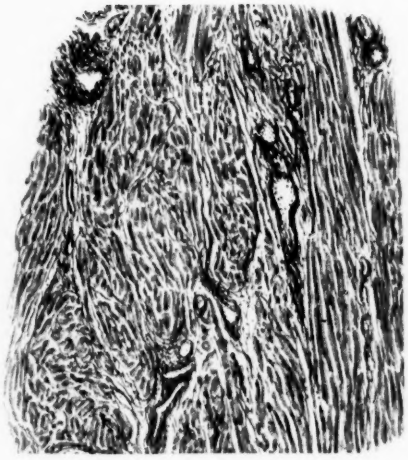

Fig. 6. Placenta acreta. Uterus, cæsarean section. Azan stain.

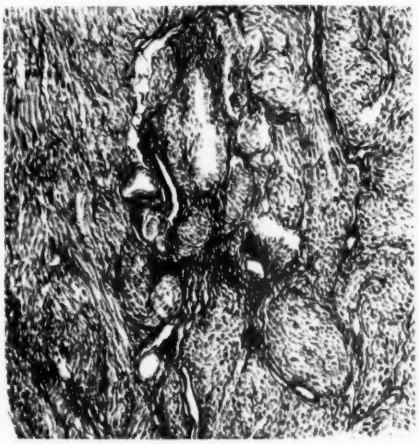

Fig. 7. Atonic uterus.

protocol number 22627. The patient was a young woman, aged 19 years, a primipara. Menses had started when she was 17 years of age. After a normal pregnancy she had had a normal delivery followed by a severe bleeding before the placenta was expressed, and this had to be done by the Credé maneuver. The vagina and uterus were douched with warm saline; the uterus massaged and a tamponade inserted into the uterus. An intravenous normal saline infusion was given, followed by a blood transfusion. In spite of all these measures the bleeding continued and the patient died 2 hours after delivery. Postmortem examination showed hyperplasia of the thymus gland. The ovaries were markedly hypoplastic. The uterine wall appeared thin, the inner surface entirely smooth without any placental tissue present. Postmortem diagnosis: atonic uterus probably due to status thymicolymphaticus.

Atonia is also spoken of as exhaustion of the uterine muscle. The Duncan separation of the placenta is thought to be a result, in most instances of uterine exhaustion thus causing the incomplete separation of the placenta and with it, the severe bleeding postpartum. Such a uterus is very large and soft, the muscle being entirely without tonus. Status thymicolymphaticus, as presented in the above case history has never been mentioned by any of the authors as a probable cause of atonia. However, such a case is prone to have hypoplastic ovaries and also a uterus which is not well developed and with poor musculature. Causes which have been cited as capable of producing uterine atonia are those producing exhaustion of the nervous mechanism governing the uterine mechanism, such as prolonged labor, loss of blood from antepartum

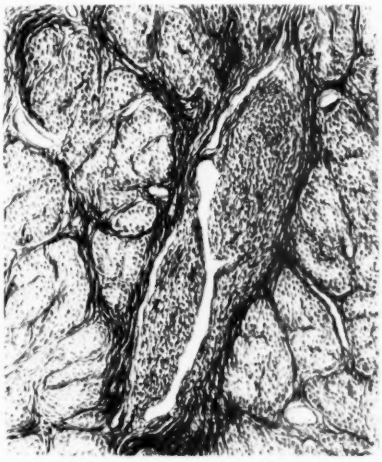

Fig. 8. Atonic uterus.

hæmorrhage, emotional causes, improper coordination of the powers, mental and nervous depression from severe pain, anxiety or shock. Antonia due to any of the above causes is aggravated by toxæmias of pregnancy. Uteri which are characterized during labor by cramp-like pains accompanied by very weak contractions, uteri which are affected by fibroids, or uteri overdistended by polyhydramnios or multiple pregnancies almost always tend to be flabby postpartum.

In Figures 7 and 8 the pathology of the fibers can be readily seen. The fibers are thin and short and have not a very good affinity for the stain. In some areas there is a slight amount, and in other areas a vast amount of intrafasicular connective tissue, but a very marked amount of interfasicular connective tissue is to be seen throughout. The average number of fibers in Figure 7 was 52.2 fibers and on another checking was found to be 52.5 fibers per millimeter. In Figure 8 the average number of fibers was 53.7 and another checking was 54.2 per millimeter.

TABULATED SUMMARY

Fig.	Average number fibers (width) per mm.	General characteristics		Amount of connective tissue	
		Length of fibers	Affinity of fibers for stain	Intrafasicular	Interfasicular
1	22.4	Long	Good	Very little	Moderate
2	30.5	Long	Good	Very little	Moderate
3	36.7	Long	Good	Very little	Scant
4	25.4	Long	Good	Very little	Scant
5	23.7	Long	Good	Very little	Scant
6	27.6	Shorter	Fair	Much	Slightly greater than normal
7	52.2 52.5	Very short	Poor	Moderate	Much
8	53.7 54.2	Very short	Poor	Moderate	Much

The above tabulated summary gives in brief the important findings in the various types of uteri studied: normal uteri removed following cæsarean section, normal uteri postpartum, a uterus removed in a postmortem cæsarean section without labor, uterus with placenta prævia, a uterus with placenta acreta, and an atonic uterus. The points compared are: the number of fibers per millimeter, the relative lengths of the fibers, and their staining ability and the amount of intrafasicular and interfasicular connective tissue.

Special thanks and gratitude are due Professor Doctor Oskar Frankl for allowing me free use of the material at his clinic and also for his invaluable advice.

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CLINICAL SURGERY

FROM THE SURGICAL SERVICES, MASSACHUSETTS GENERAL HOSPITAL

A NEW MUSCLE SPLITTING INCISION FOR RESECTION OF THE UPPER THORACIC SYMPATHETIC GANGLIA

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SINCE 1929 the writers have performed 52 resections of the upper thoracic sympathetic ganglia through the posterior thoracic route which was first suggested by Henry on anatomical grounds for the relief of angina pectoris in 1922 and later modified and first performed by Adson, who made it the standard operation for the relief of vasospasm in the upper extremity. In the beginning we performed the operation just as Adson described it, but with increasing experience we have adopted a new type of skin and muscle incision. We believe that this new modification makes for a more anatomical type of incision, that it gives a better exposure of the first or second rib, and that it obviates certain postoperative complications which will be discussed below. We have performed this operation for a variety of peripheral vascular and other conditions which have been described in previous communications (6, 7, 8, 9). It is not, therefore, our object to discuss the indications for or the results of thoracic ganglionectomy at this time, but to describe in detail the technique which we have found most satisfactory.

In the first 34 cases of this series a longitudinal incision was made in the skin exactly as described in Adson's papers (1, 2); for a bilateral sympathetic ganglionectomy the incision was made in the midline from the spinous process of the seventh cervical vertebra down to the fourth or fifth thoracic; in the case of a unilateral resection, a similar paramedian incision was made one to two fingerbreadths lateral to these spinous processes. With this approach one is forced to divide the trapezius muscle as well as the rhomboids and the serratus posterior superior directly across their fibers. We believe that such an incision is unanatomical because it produces considerable bleeding and also because muscles cut in this direction are difficult to heal. Furthermore, in using this approach it is necessary to employ prolonged forceful retraction of the muscles in order to expose and resect the first or second ribs. Such retraction traumatizes delicate muscle fibers and deprives them of their blood supply during the ensuing period of the operation. These factors, plus the use of small rubber drains in some cases, were the cause of sepsis in 29.4 per cent of the incisions made by this approach. Sepsis of this type, while never serious, lengthened the hospital stay of these patients from 1 to 3 weeks, and frequently resulted in the separation of the sutured muscles with an unsightly scar and weakness of the shoulder girdle.

In considering the best method of obviating these complications, the writers' attention was directed by Dr. E. D. Churchill to an incision recommended by Head and Bigger for extrapleural thorocoplasties of the upper three ribs.[1] We have now utilized this approach in 18 cases with only one instance of wound sepsis, which occurred in an epileptic who tore open his wound during a convulsion. All the wounds have healed with perfect apposition of the muscles which have only been divided in the plane of their fibers. Such a muscle splitting incision can be carried out with very little bleeding and the minimum of trauma to the muscles. Exposure of the first or second ribs is also facilitated by the direction of the incision, as it parallels their course; furthermore, a minimum of retraction is necessary. When the skin muscle incision has been made, resection of the proximal portion of the rib with its transverse process and exposure of the sympathetic ganglia is carried out in exactly the same way as in the operation which has been described by Adson.

[1] Since this paper has been in preparation Dr. S. C. Harvey and Dr. A. W. Oughterson, of New Haven, have informed us that they have also developed a similar oblique incision from the suggestions of Head and Bigger.

Fig. 1. The insert shows position of patient on cerebellar table. Note that three pillows under thorax and low position of head-rest give good flexion of cervicodorsal spine. The inner sides of elbows and arms should be well padded to avoid pressure paralysis. The skin incision and separation of trapezius muscle fibers are shown. The insert also shows the orientation of the incision in the following drawings.

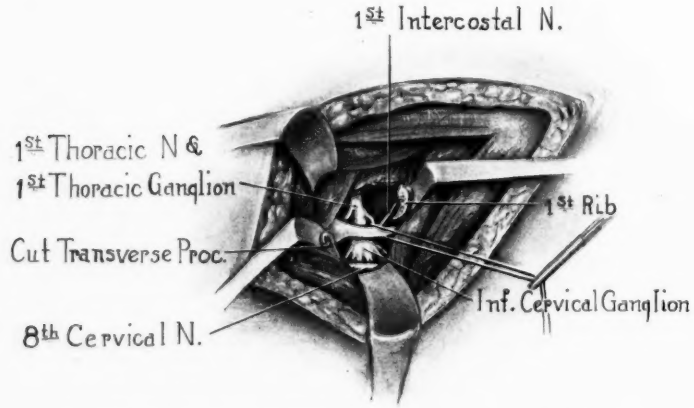

Fig. 2. The separated edges of the trapezius muscle are drawn back. The minor rhomboid has been separated from the levator anguli scapulæ muscle, while the forceps grasp one edge of the serratus posterior superior which is being split by the scissors.

TECHNIQUE OF OBLIQUE MUSCLE SPLITTING INCISION

The patient is anæsthetized with nitrous oxide, oxygen, and ether administered by a closed pressure apparatus to enable the lung to be expanded in case the pleura is opened. Intratracheal anæsthesia is the ideal method if an anæsthetist is available who is accustomed to its administration. Under these circumstances we advise avertin (tribromethyl alcohol) supplemented with nitrous gas, oxygen, and ether. The patient should be placed on a cerebellar type of operating tab with the forward curvature of the head and n k exaggerated by placing three pillows und the chest (Fig. 1). This position serves to spr d the upper intercostal spaces and to give the g atest possible abduction to the scapula. The s in incision is made starting a finger's breadth ateral to the spinous process of the seventh cervi l vertebra and running obliquely downward a l outward over the medial angle of the scapula. his incision need not be over 8 centimeters long. In the

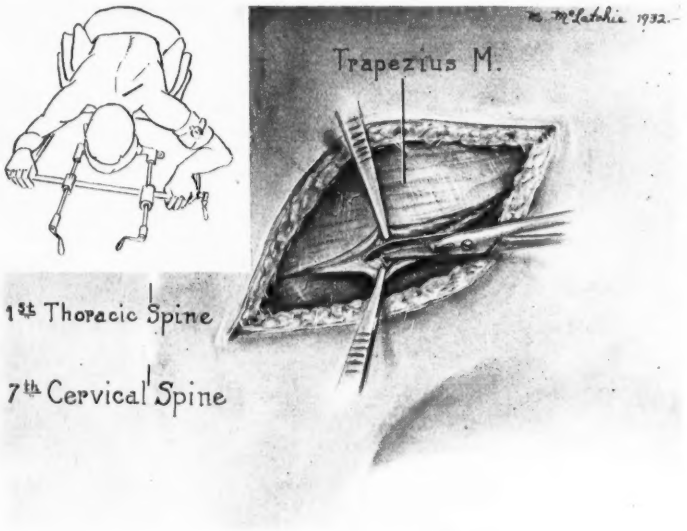

Fig. 3. All the muscles attached to the scapula have been retracted. The second rib shows in the lateral half of the field, whereas medially the rib and its transverse process are covered by the longitudinal band of the erector spinæ group of muscles.

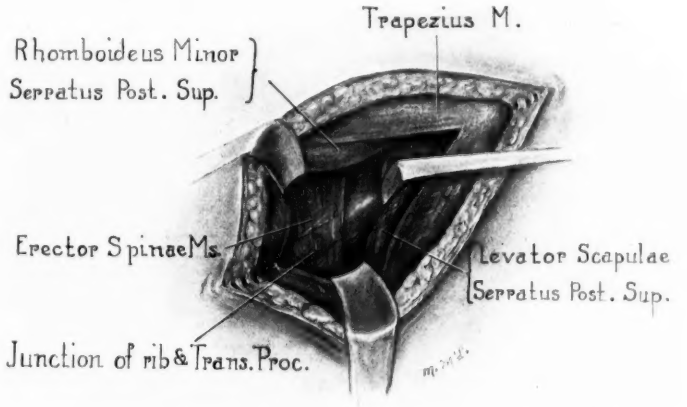

Fig. 4. Exposure of second rib, after separation of intercostal muscles and underlying pleura. Note articulation with transverse process, which must also be removed. The first and third ribs barely show in the upper and lower edges of the incision, but by suitable mobilization and retraction of the muscles they can be adequately exposed and resected.

case of a bilateral operation, a similar incision is made on the opposite side, but it is unnecessary to carry it across the midline. The cut is carried down to the deep fascia, bleeding points are ligated, and skin towels are applied. This oblique incision runs nearly parallel to the fibers of the trapezius, which are now separated by cutting through the fascia and stretching with the fingers. The fibers of the trapezius are then retracted upward and downward, thus exposing the minor

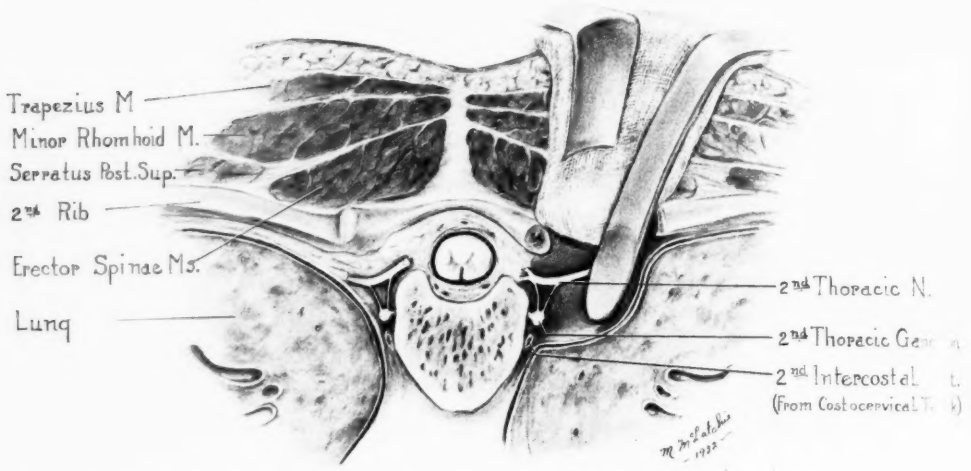

Fig. 5. Cross section of the thorax at the level of the second thoracic vertebra, to show the position of the sympathetic trunks.

rhomboid and levator anguli scapulæ muscles (Fig. 2). Separation of these is again carried out by blunt dissection and the muscles then drawn apart by a pair of retractors. At this stage the upper ribs can be palpated, being covered only by the thin fibers of the serratus posterior superior muscle (Fig. 3). On splitting its fibers, the three upper ribs and the deep longitudinal back muscles are exposed. The attachments of these deep muscles are then separated from the transverse processes of the first and second ribs and drawn back by a medial retractor (Fig. 4). The resulting exposure gives ample room for resection of the proximal portions of any of the three upper ribs. Generally speaking, we intend to remove a portion of the cervicothoracic sympathetic trunk extending from above the inferior cervical ganglion to below the second thoracic ganglion. It is easier to reach the upper portion of the trunk through the first rib and the lower portion of the trunk through the second rib. However, as a rule, this portion of the trunk can be resected through either rib. Occasionally, in difficult cases, it is best to remove both.

It is important that at least the proximal 3 centimeters of the rib and the entire transverse process should be removed. The greatest care should be exercised to leave the pleura intact, but if a small opening is made it can frequently be closed by a small piece of muscle and the lung maintained in an expanded position by warning the anæsthetist to use positive pressure. As a general rule the patient's condition does not change, but it is of the greatest importance to remember that certain types of opening in the pleura can allow more air to enter on inspiration than can leave on expiration. Even with adequate means of controlling the intratracheal pressure, the operator must be constantly on his guard against such a valve type of opening and be ready to aspirate air from the chest if the patient's blood pressure falls or cyanosis develops. If the operator is on his guard the air can easily be removed with a large syringe and needle or through a rubber catheter inserted through the hole in the pleura and connected to the suction apparatus. Such a device should be always at hand. One of the writers had a case of sudden collapse from this cause, in which over a liter of air was removed from the pleural cavity and the patient's condition immediately improved; had this not been foreseen the patient surely would have died on the table.

After removal of the rib and transverse process, the pleura is separated from the body of the vertebra with blunt dissection. For this purpose the operator's index finger is the ideal instrument. The pleura must be separated to a depth of 3 centimeters and can best be retracted by the use of a brain spoon. The best possible illumination is a requisite for this part of the operation. At this depth the sympathetic chain is usually seen un-

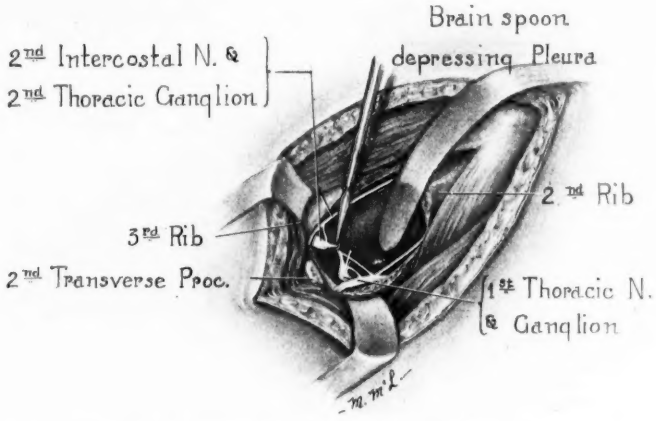

Fig. 6. Nerve structures seen after resection of second rib and transverse process.

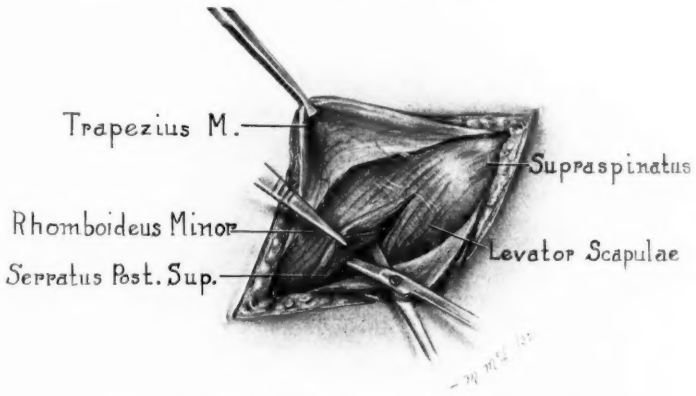

Fig. 7. Nerve structures seen after resection of first rib and transverse process. The cervicothoracic ganglion lies at a greater depth than is shown here, where it is depicted drawn up into the wound in order to show its shape and the relation of its rami.

ning longitudinally and adherent to the sides of the vertebral bodies. If it cannot be located in this way it can be found by search for the sympathetic rami, which leave the second intercostal nerve and join the sympathetic trunk about a centimeter deeper down (Fig. 5). The communicant rami of the large first thoracic nerve, which crosses the upper end of the incision, can also be used as a guide to find the sympathetic trunk, as the first thoracic ganglion lies just beneath it. Once the trunk is located, it should be drawn up on a nerve hook and followed both upward and downward by a blunt dissection (Fig. 6). Through either a first or second rib resection it is possible with care and patience to follow the trunk downward and cut it beneath the small second thoracic ganglion. Then with downward traction and by successive cutting of the small sympathetic rami as they leave the trunk, it should be possible to visualize two large ganglia higher up (Fig. 7). In our experience the stellate ganglion has usually consisted of two large and distinct components, the lower and smaller of the two lying just beneath the large first thoracic nerve, the second and larger ganglion about a centimeter above. Rarely these two ganglia may be fused into a single struc-

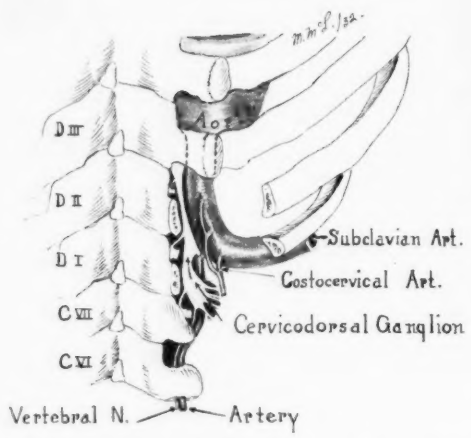

Fig. 8. Relation of the left cervicothoracic ganglion to the large arteries of the upper thorax. The descending branch of the costocervical artery, which forms the first and second intercostals, may be either superficial or deep to the sympathetic trunk. The upper end of the inferior cervical ganglion lies on the vertebral artery. The subclavian lies considerably deeper and is not likely to be seen unless the pleura is widely reflected.

ture. It is well to appreciate that the inferior cervical and upper thoracic ganglia vary greatly in size, shape, and position, and that in no two cases are these structures identical. A large ramus usually joins the first thoracic ganglion to its spinal nerve, but occasionally the ganglion and nerve are fused (a condition we have encountered in 2 of our cases). For this reason it is extremely important to have a good exposure in order to avoid injury to the first thoracic nerve with resultant partial paralysis to the arm. Even handling of this nerve should be avoided as much as possible, as this is a frequent cause of severe postoperative neuritis in the upper extremity. It is also necessary to remember that the cervicothoracic ganglion is in close relation to the large costocervical and vertebral arteries and, to a lesser degree, to the subclavian arteries (Fig. 8). Minor bleeding in this region is easily controlled by the use of dura clips, but an injury to the vertebral artery in this region would cause severe hæmorrhage. After the large ramus joining the first thoracic ganglion to its spinal nerve is cut, it is not difficult to draw the sympathetic trunk downward to a point where the inferior cervical ganglion can be safely dissected out.

The incision is closed tightly unless persistent oozing demands drainage. Otherwise we have found drains to be unnecessary and a frequent

Fig. 9. Scars of bilateral incisions. From a photograph taken 14 days after operation on the right side, 7 days after operation on the left.

cause of infection. As the retractors are removed, the muscle edges fall together and require only a few interrupted catgut sutures for perfect apposition. A row of interrupted sutures through the deep fascia of the trapezius, and silk sutures in the skin, complete the operation. The best dressing consists in silver foil covered with gauze sponges, which are held in place by crucial strips of adhesive running over the shoulder.

In this operation postoperative shock almost never occurs unless an extensive pneumothorax is allowed to develop through opening the pleura. Such an accident can usually be avoided by taking sufficient time in resecting the rib (especially in the second rib approach), and in using careful, slow, blunt separation of the pleura from the bodies of the vertebræ. Even if a pneumothorax occurs, serious complications can be avoided by its early recognition and thorough aspiration of the air. Although the patient usually shows no change in blood pressure or pulse rate, we have felt that even under the most favorable circumstances the bilateral operation should be done in two stages. With the oblique muscle splitting incision, all skin sutures can be removed within a week and the operation performed on the opposite side at the end of this interval. As neither incision is carried to the midline, the previous scar can be completely covered with the skin towels at the time of the second operation. Postoperative discomfort lasts only a few days and the patients need not be kept in bed over a week. The usual appearance of the bilateral incisions, 7 and 14 days after operation, is shown in Figure 9.

SUMMARY AND CONCLUSIONS

As the result of the recent growth in understanding of the sympathetic nervous system, the

more accurate knowledge of the ganglia which must be removed to produce a given effect and the development of improved diagnostic methods, the indications for thoracic sympathectomy have been greatly enlarged. The increasing importance of this procedure has led us to report a new oblique muscle splitting incision, which in our hands has avoided much unnecessary bleeding and trauma of the large muscles of the back. As the result of this slight technical improvement, wound healing has been greatly accelerated, sepsis and separation of the divided muscles has been practically eliminated, and access to the upper ribs and their underlying ganglia has been facilitated.

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FROM THE UNIVERSITY OF MICHIGAN HOSPITAL

TOTAL PULMONARY LOBECTOMY[1]

A Simple and Effective Two Stage Technique

JOHN ALEXANDER, M.D., F.A.C.S., Ann Arbor, Michigan

CERTAIN cases of bronchiectasis and multiple pulmonary abscess can be cured only by total removal of a lobe of the lung. The exceptional difficulty of the technical problems connected with total lobectomy is evidenced by a 53.4 per cent mortality in 127 cases that I have collected from the clinics that have not been importantly connected with the relatively recent advances in technique. Another series of 115 cases with a mortality of 21.5 per cent has been collected from the four clinics in the United States and the four in Canada and Europe that have been chiefly responsible for the present hopeful outlook for a steadily declining mortality rate and an increasing proportion of truly complete cures.

The present justifiable optimism is especially gratifying in view of the statements made by Samuel Robinson (26) in the presidential address before the 1922 meeting of the American Association for Thoracic Surgery. He said, after presenting what is undoubtedly one of the most pessimistic descriptions of the difficulties of an operation that has ever appeared in print, that "It has always been my belief that the greatest triumph in thoracic surgery will be the surgical eradication of this deplorable disease [bronchiectasis]." Tuffier, in 1924, said that he had never completely cured a case of pure bronchiectasis. Archibald, in 1927, wrote that the problem of lobectomy is chiefly concerned with the question of operative mortality and that it will be solved when the mortality has been reduced to 20 per cent or even less.

In this article I shall consider critically the various techniques that appear, on the basis of results and theory, to have the greatest promise. I shall present in detail a simple operation that seems to me to make more effective use than does any other of safeguards against the complications of shock, primary and secondary hæmorrhage, pneumonia, overwhelming infection of the pleuræ and mediastinum, mediastinal emphysema, bacteriæmia, tension pneumothorax, and mediastinal "flutter," which have been the chief reported causes of death after lobectomy.

Briefly, this operation consists, at the first stage, in resection of the posterior portions of the sixth, seventh, and eighth ribs, separation of the diseased lobe from any pleural adhesions, gentle stroking with gauze of the parietal and visceral pleur of the whole hemithorax in order to create a pr tective inflammatory barrier against subsequer infection and to cause the undiseased lobe to b come adherent, and the placing of an air-tig drain. At the second stage 9 to 12 days later, t incision is reopened, only the diseased lobe is fre from its new adhesions and the hilum of the lu is tightly ligated with silk and a rubber tube a the lobe is left in place until it comes away spo taneously. The incision is closed temporarily o if the mediastinum is rigid, it is left wide open.

I have personally performed 18 total lobect mies with 3 deaths (16.6 per cent). Two of the operations were performed early in my experien by a technique (one stage in the presence of a no adherent undiseased lobe) that I soon learned to consider as unsound and one of the patients died. The remaining 16 had adhesions over both the diseased and undiseased lobes at the time the lobectomy phase of the operation was carried out and 2 (12.5 per cent) died. Twelve patients (Table I) had few or no adhesions over the undiseased lobe at the time of the first of a two stage operation, performed according to the most important of the principles that will be discussed, and 2 (16.6 per cent) died. Only the last 6 of these 12 received in more or less full measure the benefits of the operative technique that has finally been developed and none of them died. The results can now be judged in 11 of the 12 patients; all of the 9 living patients (81.8 per cent) are either complet ly cured or improved.

INDICATIONS

This article is concerned with total lobecto y as indicated for the common central type of br nchiectasis or for extensive multiple pulmonary b scesses, perhaps associated with bronchiect s, and without inseparable pleural adhesions. It should also be useful for pulmonary neopla ns that do not require complete resection of the l ar bronchus; for those that do, I believe that he technique to be described by Churchill (12) is be er.

Consideration will not be given to partial l ctomy as indicated for extracentral caver us

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lions involving the parenchyma and bronchi. There are frequently extensive pleural adhesions over such lesions and in this type of suppuration I have found the Evarts Graham partial cautery lobectomy to be of great value. Graham (5) has used this operation in 54 patients with only 6 operative deaths (11 per cent). The partial lobectomy advocated by Brauer seems to me less safe.

Elsewhere, Alexander and Buckingham have discussed somewhat fully the management of various types and phases of non-tuberculous pulmonary suppuration and considered the indications for total lobectomy. Briefly, the patient and particularly his cardiocirculatory system must be in reasonably good condition, and his disease should be known to be confined to one lobe as determined by lipiodol roentgenograms of all five lobes. In 4 of the 18 cases reported in this article, lateral and anteroposterior bronchograms, in which lipiodol appeared to have entered the upper as well as the lower lobe, seemed to indicate that the lesions were confined to the lower lobe and yet, after basal lobectomy, additional bronchograms showed that there remained bronchiectasis in the upper lobe. This diagnostic mistake was occasioned by either of two errors: (1) Bronchiectasis which appeared in the postero-anterior bronchogram only as high as the fourth rib posteriorly was interpreted as occupying the apex of the lower lobe, whereas it was actually in the mid-portion of the upper lobe. The lateral bronchograms were of relatively little value at this high level. (2) Bronchiectasis, which appeared in the lateral bronchogram in the left lower midaxillary line, was interpreted as occupying the anterior portion of the lower lobe whereas it actually occupied the lingula of the upper lobe (first ventral branch of the upper lobe bronchus). The corresponding involvement on the right side is of the middle lobe and is more readily diagnosed in a lateral bronchogram.

Certain therapeutic measures should be given adequate trial, for months or even a year or more, before a decision is made to perform a lobectomy. Most important among these are phrenicectomy (perhaps temporary phrenic nerve interruption is preferable, as suggested by Churchill, 11); a modified sanatorium regimen; postural drainage every 2 or 3 hours during the patient's waking hours; conservative treatment of sinus, ear, and mouth infections; one or more courses of bronchoscopic aspirations and possibly intravenous neosalvarsan injections. Some or all of these measures were used in each of the cases reported in this article before a decision to perform a lobectomy was reached.

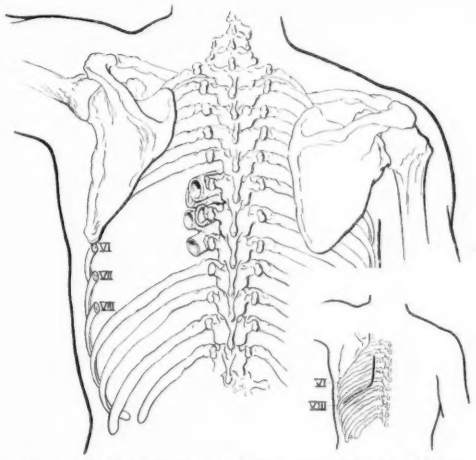

Fig. 1. Indicating extent of ribs resected for basal lobectomy and relation of operative window to hilum of lung. Inset shows position of incision.

THE OPERATION

Pre-operative management. In the technique about to be described it is important that the sixth, seventh, and eighth ribs be exactly identified for resection because they immediately overlie the hilum of the lung. It is, therefore, necessary to know before the operation is begun whether the lowest rib that is palpable in the loin is the eleventh or the twelfth so that a beginning may be made for an accurate count upward. This knowledge may be got either from a roentgenogram that shows all of the ribs or by counting the ribs, before the patient is draped, downward from the readily identified second, opposite the angle of Louis.

Shortly before operation, the patient empties his lung of secretions as completely as possible. A small dose of pantopon or morphine without atropine is given before operation.

The patient is placed on his "good side" on the operating table in not less than 15 degrees Trendelenburg position. I rely upon this position and occasional aspiration of secretions from the mouth rather than upon intratracheal aspiration through a tube which, I believe, dams back some of the secretions at the rima glottidis. The Trendelenburg position helps the secretions to gravitate toward the mouth, and light doses of morphine and nitrous oxide do not abolish the cough reflex. These important precautions reduce the chance of postoperative pneumonia; this complication occurred only once among my patients and in that instance was not fatal.

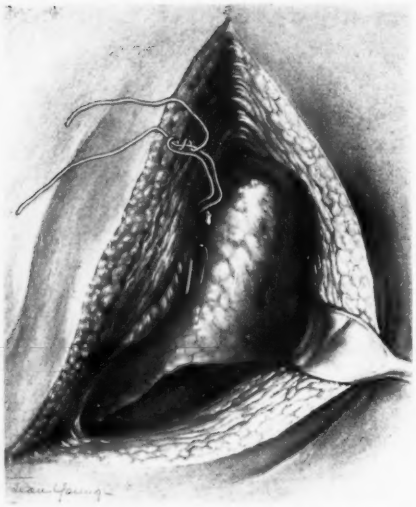

Fig. 2. Simple encircling ligature of hilum of lower lobe is about to be tied close to pericardium. This is done by touch because even the partially deflated lobe obscures the hilum. For clarity, the drawing shows the lobular pulmonary markings and the layers of the wound in the thoracic wall. Actually these are hidden at this stage of the operation by the traumatic inflammatory reaction produced by the first operation.

First stage. Local anæsthesia is used until the pleural cavity has been opened, and then light positive pressure nitrous-oxide-oxygen is given through a snugly fitting mask. The incision for the usual basal lobe lobectomy is made from the angles of the fifth to the ninth ribs and then over the eighth intercostal space to the posterior axillary line (Fig. 1). If the cutaneous incision is made more posteriorly, the sacrospinalis muscle will be left bare after the second stage. The sixth, seventh, and eighth ribs and the sixth and seventh intercostal bundles are resected from the very tips of the vertebral transverse processes to the posterior axillary line. The parietal pleura is widely incised, and if pleural adhesions over the diseased lobe seem probably separable, the bared sheet of parietal pleura is cut completely away between the fifth and ninth ribs and between the transverse processes and the posterior axillary line, so as to give free access to the lung. Its retention would serve no purpose. "Rib spreaders" are placed.

It is not possible to tell before operation how extensive pleural adhesions are unless a pneumothorax is induced and this is usually inadvisable (yet Brunn (8) has found it advantageous in expelling secretions before a lobectomy operation) because of the danger of a complicating empyema. Furthermore, a pneumothorax would be unable to show whether or not adhesions, if present, might be separated surgically. The diseased lobe of my last patient was completely invested in adhesions, most of which were broken without difficulty by the fingers. The fingers are used to rupture only such delicate adhesions as would not cause even tiny tears in the lung with possible resulting pleural infection, which would certainly be a grave complication at this stage. Adhesions in the interlobar fissure are usually firmest at its costal surface and I have found it useful to open the fissure sufficiently to admit a finger into the interlobar space; the finger can usually easily separate the lobes up to the adhesions between them at their costal surfaces and these may then be divided accurately and quickly with scissors. Scissors should be used to divide other tough adhesions which are frequently met in the costovertebral gutter and between the lung and diaphragm and occasionally between the lung and pericardium. The upper lobe is usually free of adhesions. If, as occasionally happens, the adhesions investing the diseased lobe are very tough and extensive and their division is difficult and slow, I believe that the operation should be abandoned and Graham's cautery pneumonectomy resorted to. I lost a patient because of unwisely attempting to divide such adhesions.

The free edge of the pulmonary ligament should be divided with scissors and the rest of the ligament safely torn with a finger up to the inferior pulmonary vein. The less accessible portions of the pleural cavity may be better exposed by very gently retracting part of the lobe held by one or two Duval pulmonary forceps which occlude working space far less than a retracting hand.

In bronchiectasis of the large central bronchi without complicating infection and induration of the pulmonary parenchyma, the diseased lobe may be soft and have a normal appearance. In fact, a distinguished thoracic surgeon has reported that this phenomenon once so confused him that he mistook the diaphragm for the diseased lobe (which was non-adherent) and began to dissect it from the thoracic wall before he discovered his mistake. On the contrary, fibrous pneumonitis may cause such shrinkage of the lobe, and compensatory emphysema of the neighboring lobe or lobes may so cover the diseased lobe, that its identification may be momentarily difficult.

The next step in the operation is very gentle stroking of every portion of the mediastinal, costal, diaphragmatic, and visceral (except that of the

Fig. 3. About 3 weeks after total basal lobectomy in 5-year-old boy. At right, detail of wound. The great pleural hole that was occupied by the lobe has rapidly decreased by expansion of upper lobe, rise of diaphragm (q.v.) and slightly by displacement of mediastinum. Two bronchial mouths are plainly visible. The small opening below the main wound is where air-tight drainage tube had been placed at bottom of costophrenic sinus, which has now become obliterated by adhesions.

diseased lobe) pleuræ with dry gauze held on the fingers. Especial attention should be paid to the region of the hilum and to the visceral and parietal pleuræ of the undiseased lobe. The dome of the pleura may easily be reached through the operative wound.

Three objects of paramount importance are attained by stroking the pleura:

1. A sterile traumatic inflammatory exudate is produced on and under the pleura, which exudate serves as a protective barrier against the infection that will inevitably occur within the pleural cavity after the second stage of the operation. This barrier tends to prevent the virulent phlegmonous type of pleural infection, which may be complicated by mediastinitis and septicæmia, that has occurred with fatal results in so many reported cases of lobectomy in which the highly virulent organisms of the bronchiectatic secretions have been allowed to come in contact with a wholly or inadequately prepared pleura. Evarts Graham, in 1923, recognized the importance of creating a leucocytic wall in the mediastinal pleura and of causing the undiseased lobe to become adherent before the diseased lobe was removed; he used Robinson's gauze packing around the diseased lobe and left a clamp on the hilum for 3 or 4 days after the lobe was resected but apparently he was dissatisfied with the method and abandoned it.

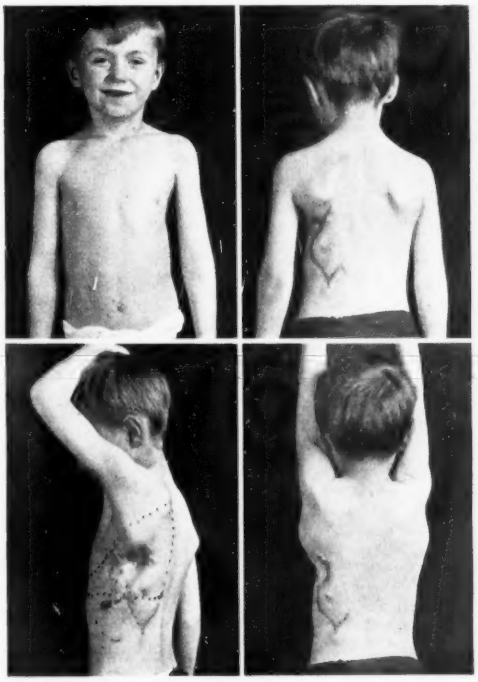

Fig. 4. Boy, 5 years old, after solid closure of wound following total basal lobectomy 6 months ago. Incision below main scar was made to obtain pedicled latissimus dorsii graft to close bronchial fistulæ. Dotted lines in lateral view represent original outlines of lower lobe.

2. During the 10 or 12 days that intervene between the first and second stages of the operation, the traumatic pleuritis results in firm adhesion between the entire lung and its investing parietal pleura. At 10 or 12 days these adhesions are not so well organized as to prevent manual separation of the diseased lobe for the purpose of the operation, and yet they are sufficiently firm to hold the undiseased lobe snugly to the thoracic wall. This fixation of the undiseased lobe limits the empyema that develops after the second stage to one-half of the pleural cavity and this empyema cavity becomes obliterated spontaneously. If the empyema should occupy the entire pleural cavity, as it does after a one stage lobectomy in the presence of a non-adherent undiseased lobe if pleural infection occurs, it would be a grave and perhaps fatal complication, especially in view of the large bronchial fistula that is usually present after removal of the lobe. Such an empyema is not likely to become cured spontaneously and may eventually require

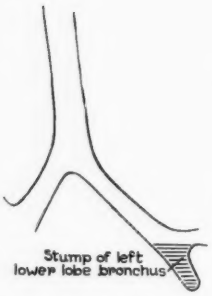

Fig. 5.

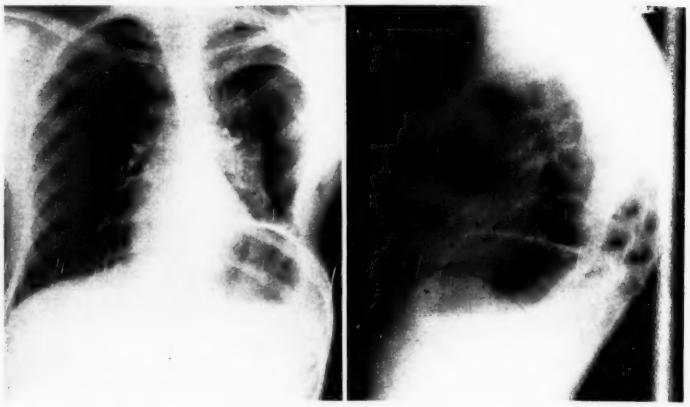

Fig. 6.

Fig. 5. Tracing of trachea and main bronchi from bronchogram of child made after closure of wound following left basal lobectomy. Iodized oil has temporarily collected in stump of left basal bronchus.

Fig. 6. Roentgenograms after solid healing of wound following total left basal lobectomy. Space once occupied by lower lobe has been filled by expansion of upper lobe and rise of paralyzed hemidiaphragm and slightly by displacement of mediastinum and depression of soft parts into defect left by removal of posterior portions of sixth, seventh, and eighth ribs. Arrows on postero-anterior exposure indicate the mesial ridge of the closed thoracic wall defect and the arrows on the lateral exposure indicate the raised diaphragm.

extensive, dangerous, and deforming Schede thoracoplastic operations.

3. A vitally important effect of having caused firm adhesion between the undiseased lobe and thoracic wall is stabilization of the mediastinum, which is contributed to by the stiffening of its pleura and subpleural tissues that follows gauze stroking of the mediastinal pleura. Stabilization of the mediastinum prevents the mediastinal shift to the opposite side and the "flutter" that have been responsible for the fatal outcome of so many reported lobectomies.

I feel that the method I have just described for treating the pleuræ is the chief cause of the success of my lobectomies. It is the outcome of a series of experiments that I performed on 16 dogs in 1921. I was stimulated to carry out this work by reading the sound opinions published by Samuel Robinson, in 1917, and by a letter received from him in February, 1921, in which he encouraged me to try to find a solution to the pleural problems.

From these experiments I found that the most effective method that I used to cause pleural adhesions was by rubbing the pleuræ with gauze and lightly scratching them with the tip of a needle or scalpel. This sometimes caused traumatic pneumonia and sometimes the scratching allowed air to escape from the lung which would have been dangerous if the lung were severely infected. In man, therefore, I did not scarify, and instead of rubbing the pleuræ, I gently stroked them and no pneumonia or pleural infection have resulted (except the contralateral non-fatal case already cited). In dogs I found that neither pneumonopexy or treatment of the pleuræ with such chemicals as tincture of iodine, 0.5 per cent silver nitrate, 20 per cent Sudan III in liquid paraffin, and ether was satisfactory. For example, in one dog 7.5 cubic centimeters of 7½ per cent tincture of iodine introduced into one open pleural cavity caused death in less than 1 minute from what appeared to be true pleural shock. In another dog 5 cubic centimeters caused death in 11 days from a violent pleuritis and pulmonary congestion and œdema. Three cubic centimeters of 0.5 per cent silver nitrate caused death in about 22 hours from a hemorrhagic pleuritis and congestion and œdema of the lungs. Because of such results as these, I feel that gently stroking the pleuræ is safer than the use of chemicals, although it is true that the amounts used were relatively greater than would be used in man and that a dog's lung is more delicate than a man's. Lilienthal in his book, published in 1925, described roughing the pleura with gauze and painting with tincture of iodine but found that firmer adhesions were formed if iodoform gauze strips were laid over the undissected lobe and withdrawn 48 hours later. Robinson (23, 24) attempted with only partial success to obtain mediastinal adhesions and fixation by packing

gauze around the diseased lobe at the second stage of a three stage operation, if the patient's condition made completion of the operation in two stages inadvisable. Evarts Graham (16) used the same method.

Stroking the pleura with gauze causes a traumatic effusion, totaling from 400 to 1000 cubic centimeters or more, which must be aspirated several times during the following week, if tube drainage is not used. Some of the fluid often becomes encapsulated in various portions of the pleural cavity and, therefore, is not removed by thoracocentesis in one place. If one of the pockets is between the undiseased upper lobe and the thoracic wall and is opened at the time of the second stage operation, a partial upper thoracic empyema results and complicates convalescence. Therefore, in order to provide constant, rather than intermittent, drainage for the effusion that forms and for whatever air may have been trapped in the pleural cavity as the wound was closed, I shall in my next patient (in the past I have used drainage only after the second stage) introduce a fenestrated rubber tube 10 centimeters into the pleural cavity through the intercostal space that lies over the bottom of the posterior costophrenic sinus and couple this tube with a long tube whose free end will be kept anchored beneath sterile solution in a bottle under the patient's bed. So that this drainage system will remain absolutely airtight until several days after the second stage of the operation, the tube should be introduced through the thoracic wall by making a stab wound no wider than the diameter of the tube, after the skin and extracostal muscles have been pushed far upward. The tube should be drawn through the stab wound by a hæmostat and when the extracostal soft parts slip down over the tube, this will then pass quite obliquely through the thoracic wall, thereby importantly helping to prevent sucking of air into the thorax around the tube.

The next step in the operation is to close the latissimus dorsi and rhomboideus major muscles with an interrupted continuous stitch of No. 1 chromic catgut, and the skin with interrupted silk, without direct drainage of the wound. Just before the last knot of the muscle stitch is tied, the anæsthetist completely expands the lung by raising the gas pressure. A vaselined dressing is placed and the incision is well supported by an elastikon dressing.

As the patient awakes from the gas anæsthetic he is made to expectorate all loose secretions from his mouth and tracheobronchial tree before he is changed from the Trendelenburg position on the operating table.

The systolic blood pressure increased during the operation an average of 21 millimeters in all of the patients operated on according to approximately this technique except that in 2 patients it dropped 28 and 20 millimeters. There was an average increase in pulse during the operation of 14.3 beats per minute. The average complete operating time was 63 minutes.

Postoperative management (first stage). Such doses of opiates should be used as to relieve pain sufficiently to make the patient willing to cough and yet not large enough to abolish his cough reflex.

Postural drainage should be continued throughout the interval between stages and should be begun within 2 or 3 hours after operation, and inhalations of carbon dioxide and oxygen should be given if needed to aid coughing and expectorating. Occasionally I have used postural drainage immediately after operation by placing the operating table in full Trendelenburg position or by inverting the patient over the edge of the table if he is unable voluntarily to expectorate his loose secretions.

Following operation the blood pressure is usually well maintained, but for several days the pulse is likely to be rapid, and occasionally is as high as 148 and even 158, and the respiratory rate is usually moderately increased. The temperature does not reach 101 degrees and as a rule is considerably less. Usually my patients get out of bed for a few minutes 8 or 10 days after operation.

The second stage should be performed 9, 10, 11, or 12 days after the first stage. If performed sooner than 9 days the pleural adhesions of the undiseased lobe are not likely to be strong enough to keep this lobe from retracting from the thoracic wall, whereas after 12 days the adhesions of the diseased lobe may be too tough to permit their rupture by the operator's fingers. If 3 or even 4 weeks were allowed to elapse between stages, instead of 10 or 12 days, the pleura would be still thicker and a correspondingly more effective barrier would exist between the body and the empyema that follows the second stage operation, and the mediastinum would be still more rigid and undoubtedly sufficiently so to make it perfectly safe to leave the thoracic wall wound wide open after the second stage. This would be of advantage in controlling infection as the gangrenous lobe could be packed off with acriflavine gauze every 24 hours, or even every 12 hours, whereas this is not done for 2 or 3 days if the incision is temporarily closed. I believe that such an interval between stages would be feasible if at the time of the first stage the diseased lobe were completely

surrounded by rubber dam (Lilienthal, 18) in which there were several small dependent holes for escape of fluid, in order to prevent its adhesion to the parietes. I shall use this modification for my next lobectomy patient. Additional advantages of this will be considered in the next section.

Second stage. Pre-operative postural drainage and medication and the position of the patient on the operating table are the same as have been described for the first stage. Slightly positive pressure nitrous oxide oxygen anæsthesia is used so as to keep the newly adherent undiseased lobe from retracting from the thoracic wall. If there had been a three or four week interval between stages positive pressure would be unnecessary.

With the fingers the incision is reopened and the diseased lobe is completely freed from its adhesions. The oblique main interlobar fissure must first be identified beneath the pleural exudate so as to avoid freeing any of the undiseased lobe. It should be remembered that the normal sized lower lobe is of great height, extending from the fourth to the tenth or eleventh ribs in the paravertebral line (Fig. 4).

A liver needle threaded with 80 centimeters of very heavy braided silk of great tensile strength and which has been boiled only once is held in the fingers, rather than in a needle holder, for greater delicacy of touch and is passed without force through the hilum of the diseased lobe close to the pericardium. Here the hilum is about 3.5 centimeters broad and the needle passes through it at approximately the junction of its upper quarter and lower three-quarters. The needle should not and probably does not pass among the great vessels and bronchus but above them, through the lower part of the web of parenchyma that lies between the lobes.

After the needle has been passed, the silk is divided at its middle and one half is then tied with a surgeon's knot as tightly as possible around the upper part of the hilum and the other half around the lower part. Each pair of ligatures is then made to encircle the whole hilum and is tied tightly.

The method of hilar ligation just described is the one that I have used until now. When, in my earlier cases, the ends of the tied ligatures were passed through the latissimus dorsi muscle in order to exteriorize the lobe, it was important that a transfixion ligature be used to prevent slipping. But as I no longer exteriorize the lobe nor resect it immediately after ligation, this is not necessary. Two or three superimposed simple encircling ligatures of heavy braided silk with surgeon's knots (Fig. 2) should be as effective as a transfixion ligature and be without the potential danger of the latter. Encircling ligatures placed close to the pericardium of a fresh cadaver did not tend to slip distally. I shall use them for my next patient.

On several occasions I found that these tight ligatures of the indurated hilum did not completely shut off the blood supply to the lobes which remained partially viable and later needed to be removed with the actual cautery, in one or more stages, between which, in one patient, there was a small hæmorrhage from the stump. I have heard of one and possibly two sudden deaths that were apparently due to resection of the lobe with an electric cutting current.

On two or three occasions I found that the ligatures occluded the pulmonary vein but not the artery, and wet rather than dry gangrene resulted with great exudation of blood into the lobe and leakage of much bloody serum from it, requiring blood transfusion. In these patients the artery was closed by ligating the hilum, the lobe still being in place, with a live rubber tube (Lenhartz). It may be necessary to retie this tube more tightly each day for several days. In the future I shall apply this elastic ligature during the second stage operation, immediately after ligating with silk. I doubt if the elastic ligature alone could be counted upon immediately to occlude both artery and vein, unless the hilum were first tightly tied with silk.

In none of my patients has there been any known reflex cardiac or respiratory disturbance from tight ligation of the hilum close to the pericardium and in only the first 1 or 2 cases did I first inject procaine around the hilum. I have crushed the hilum before ligating in only one case and there was no ill effect, but since then I have felt that the risk of causing a fatal reflex or of fracturing a part of the hilum was greater than the obvious advantage of crushing the infiltrated hilum so that the ligatures would more surely occlude the vessels and bronchus. Morrison found in experimenting upon rabbits that crushing and ligating the hilum of one lobe caused no important reflex disturbance but that crushing the whole hilum of a lung caused almost immediate death unless the vagus nerve had been divided or blocked. He states that other experimenters found that this reflex did not occur if the whole hilum had been only ligated and not crushed.

I feel very strongly that it is better not to cut away the lobe after ligating its hilum but to leave it until it spontaneously separates at the line of demarcation at the ligatures, from 10 to 20 days after operation, or at least not to cut it away until a week or 10 days after operation. It is, of course, unpleasant to have a pulpy gangrenous lobe attached to the body for days but there are two very

real dangers of removing the lobe during the first postoperative week: If the hilar ligatures have not completely closed the vessels and bronchus, these will leak blood, bronchial secretions, and air into the pleural cavity and the leakage of air might cause a fatal tension pneumothorax if the thoracic wall incision were closed and if the drainage tube should have become plugged. Even if the hilar ligatures completely occluded the vessels and bronchus at the time of removal of the lobe, there is a tendency for the ligatures to loosen because of pressure necrosis of the ligated tissues and because of the infection that is present in the hilar stump. A fatal secondary hæmorrhage or embolus to the brain or tension pneumothorax might be the result. Garrè and many others who amputate the lobe, ligate separately any vessels they find on the cut surface of the stump to help to avoid the danger of secondary hæmorrhage. It seems likely that there is a better chance of the thrombi that form in the vessels becoming solidly organized if the blood vessels are not cut across and their open lumens directly exposed within a week of the hilar ligation. The ligatures around the blood vessels are not a permanent barrier of protection to the thrombi central to the ligatures against the infection in the thrombi distal to the ligatures. Infection of the thrombi central to the ligatures would of course expose the patient to the dangers of secondary hæmorrhage, embolism, and bacteriæmia.

It seems reasonable to assume that primary resection of the lobe, with the considerable manipulation of the stump that the ligations and layered suture entail, exposes the patient to greater danger of embolism and brain abscess than if the hilum were merely ligated. Two of 46 patients operated on by several surgeons according to the Shenstone technique, died from brain abscess.

Whittemore (36, 37) in a one stage operation deeply sutures the lung, as near to the hilum as possible, to the extracostal muscles (and occasionally also ligates the hilum with a catheter) thereby steadying the mediastinum and, as the lobe is not removed during the operation, allowing infection to set in gradually. He has had 3 deaths among 10 patients. The fundamental principles of the Whittemore operation appeared to me as sound but my early actual experience with it dissatisfied me and I lost one of the two patients for whom I used it. My chief objections to it are these: (1) Infection of the entire pleural cavity is almost inevitable within a week of operation, by which time the sutures uniting the lung and extracostal muscles will have loosened, allowing the infected lung to slip into the pleural cavity which has not been adequately prepared for so severe an infection. And as the undiseased lobe has scarcely had time to become firmly adherent to the thoracic wall, or the mediastinum to become fairly rigid, the open pneumothorax, that occurs when the lung retracts from the thoracic wall, may prove fatal in itself or through a pneumonia which such a pneumothorax favors. (2) Even the partial exteriorization of a lobe, without the addition of a quite extensive thoracoplasty to cause the thoracic wall to drop well inward, produces traction upon the heart and great vessels of the mediastinum (Bolgiano, Patek and Sailer; Sauerbruch and Robinson). It is difficult for the surgeon to predict whether or not the traction that he exerts upon the mediastinum in fixing the lobe in a more or less exteriorized position, will cause dangerous disturbances of the cardiocirculatory system. In 2 of my patients I felt within 48 hours of operation that the traction was too great and so cut the sutures that were holding the partially exteriorized lobe to the thoracic wall.

In most of my two stage lobectomies I have exteriorized the lobe at the second operation. However, during recent months I have felt that in view of preparation of the pleura for infection and against "mediastinal flutter" at the first stage that exteriorization of the lobe at the second stage was not only potentially dangerous but entirely unnecessary. Therefore, in my last two patients I left the diseased lobe after ligation of its hilum, in the pleural cavity and closed the thoracic wall incision tightly, leaving an air-tight drainage tube in the position described under "first stage." My present technique, therefore, has no relationship with the Whittemore technique.

The wound in my last two patients was closed airtight so as to protect them against any harmful respiratory mediastinal movement that might possibly have occurred during the first 2 or 3 days after operation if the incision had been left open, because the gauze stroking of the mediastinal pleura 12 days before might not have sufficiently stiffened it. A catheter, whose outer end was clamped, was introduced into the lower pleural cavity alongside of the lobe for intermittent installations of Dakin's solution. Two or 3 days after operation, which was 2 or more days before the bronchus might be expected to open spontaneously, the incision was completely reopened, as had been intended, and the pleural space around the gangrenous lobe was loosely packed daily with acriflavine gauze until the lobe was removed about a week later. This procedure proved to be entirely satisfactory. Theoretically it would be preferable not to close the incision at all after the second

operation but to keep the lobe available for inspection at any time so as to detect at once signs of wet rather than dry gangrene, any bleeding from the crushed hilum where it was crushed by ligation, and also to eliminate the possibility of a tension pneumothorax that might arise from a known or unknown opening of any part of the lung. With a closed incision, bleeding would be detected and a tension pneumothorax prevented if the air-tight drainage tube were open but, if the tube had become plugged, the diagnosis might be made too late. I believe that it will prove perfectly safe to leave the incision wide open after the second operation is completed if 3 weeks are allowed to elapse between the first and second stages so as to give the mediastinum plenty of time to become quite rigid. This interval of time should be possible if the lower lobe is surrounded by rubber dam at the first stage operation. The advantages of a 3 week interval between stages and of leaving the wound open after the second stage, so as better to control infection, were discussed in the last paragraph of the section, "postoperative management (first stage)."

The patient is made to cough and expectorate before the Trendelenburg position of the operating table is changed.

The majority of the second stage operations have been performed in 35 minutes or less, from beginning to end. In most of the patients the systolic blood pressure was higher at the end of the operation than at the beginning; in the rest the drop was 10 millimeters or less, except that in one patient it dropped from 126 to 112. The pulse rose during the operation from an average of 124 to 139. The greatest increases were from 112 to 162, which 2 hours later was 136, and from 132 to 164, which 5 hours later was 120. There was usually an increase during operation of 10 or 20 and occasionally even more in the respiratory rate which decreased slowly during the following days.

Postoperative management (second stage). Opiates and carbon-dioxide inhalations are given as after the first stage and regular postural drainages are used for at least several days until normal expectoration can be counted upon to clear the lungs of secretion and thereby reduce the chance of pneumonia. For a day or so the sputum may be somewhat bloody due to trauma to the bronchial mucosa by the hilar ligatures. Instillations of 60 cubic centimeters of Dakin's solution through the catheter are begun immediately after operation and continued every 2 hours until the incision is reopened 2 or 3 days later when acriflavine gauze, in which several Dakin's tubes are held, is snugly packed around the gangrenous lobe and renewed every 12 or 24 hours. Acriflavine solution is instilled into the Dakin's tubes rather than Dakin's solution which might be harmful to the bronchus after it opens from 4 to 7 days after operation.

If the lobe is seen to be very dark and swollen an additional ligature of silk or rubber tube, or preferably both, should be placed around the hilum so as completely to close the lobar or bronchial artery. A dry gangrenous lobe is small, shrivelled, and not tense. The lobe may be left until it falls away spontaneously in from 10 to 20 days, perhaps even then requiring cutting of the tough bronchus, or the gangrenous lobe may be cut off with scissors several centimeters distal to the hilar ligatures in not less than a week after operation.

After all of the gangrenous stump has been discharged, the granulating wound should be inspected to see if any of the ligatures remain attached and, if so, gently removed. The originally air-tight drainage tube should be gradually withdrawn.

Until the pleural hole and bronchial opening or openings are completely closed, the hole should be well packed with gauze. This not only prevents pocketing off of pleural abscesses but, very importantly, occludes the open bronchi, thereby enabling the patient to expectorate effectively.

The great hole that was occupied by the lobe decreases in size with surprising rapidity owing to compensatory emphysema of the remaining lobe, to the progressive rise of the paralyzed diaphragm, and to a slight extent to shifting of the mediastinum (Fig. 6). After 2, 3, or 4 months only a saucer-like depression, with one, two, or three bronchial openings, remains (Fig. 3). As soon as the sputum becomes scanty and no longer purulent, the mouths of the bronchi should be touched with 40 per cent silver nitrate solution every 7 or 10 days. This alone may cause complete closure of the bronchi and epithelization then soon becomes complete. If, however, the bronchi resist closure by this treatment and if, 3 or more months after operation, the sputum has disappeared and only a little clear mucus is being discharged from the bronchi, the bronchi and the wound can almost always be closed by a plastic operation (Fig. 4). Either a pedicled skin flap or a large latissimus dorsi graft, which is left attached at the anteroinferior rim of the thoracic wall defect, is turned over onto the open bronchi and covered by suturing together the edges of the original cutaneous incision, after excision of scar tissue; pressure is applied by the use of a snug dressing over a rubber bath sponge.

Purulent sputum is likely to persist for several weeks after the second stage operation. Until the hilar bronchus opens several days after operation much of this sputum may come from the diseased lobe itself because its stiff walled bronchus in an infiltrated hilum may have resisted complete occlusion by the hilar ligatures. After this period, some purulent or mucopurulent sputum may persist for several weeks. It probably comes in part from inflammation of the bronchi and trachea that was a complicating part of the bronchiectatic disease, and in part from irritation of the exposed bronchial mucosa by the gauze packing. After removal of the diseased bronchi, the bronchial and tracheal mucosa gradually becomes healthy and sputum disappears.

The temperature and pulse are likely to be high for approximately 1 week after the second stage operation, the temperature usually being between 101 and 103 degrees and the pulse between 130 and 150, after which they gradually decline to normal, though the pulse may remain somewhat elevated for weeks. Sometimes the temperature may become almost normal within 2 or 4 days, and sometimes there may be considerable fever for several weeks.

Owing to the severe reaction of most of the patients to the second stage and to the high fever and debilitating effects of both the disease and the operations, one or more blood transfusions have usually been given after the second operation and occasionally before either operation. Heliotherapy has sometimes been used during convalescence and exercises given to help to prevent scoliosis. This has occurred to an important degree in only 2 patients, in 1 of whom it is severe, but this patient is comfortable and goes to school and does farm chores; the other does heavy labor with a circus.

The postoperative defect in the thoracic wall where portions of three ribs have been removed is a relatively small one and cannot fairly be called a "deformity" (Fig. 4). Bronchoscopy or a bronchogram (Fig. 5) shows the remains of the lower lobe bronchus to be a short cul-de-sac, or a two-horned cul-de-sac if the lobe were resected just distal to the first lobar bronchial division. Good drainage toward the trachea, ciliary action, and the bechic blast probably combine to keep this short stump free of bronchial secretions.

The technique that has been described has been evolved slowly from animal experiments that were begun 11 years ago and from experience with total lobectomy in man which began more than 4 years ago. Many staged cautery lobectomy has already been considered. My first experience with an initial attack upon the hilum was in a patient whose upper lobe was not adherent and for whom I performed the one stage exteriorization described by Whittemore (36). This patient died 8½ hours after operation with the appearance of shock, part of which I now feel was due to undue traction upon the mediastinal structures by way of the exteriorized lobe. The same technique was used for the next patient. The lobe became only partly gangrenous and the viable remains were destroyed by the actual cautery in several stages. The patient is absolutely well. The next 5 patients were operated on according to suggestions that had been made by Samuel Robinson (23). In 1 of these patients the parietal pleura was merely exposed and the wound closed at the first stage; in 3 a gauze pack was placed on the parietal pleura before the wound was closed and in 1 the pleural cavity was opened and gauze placed around the diseased lobe until the second operation was performed 3 days later. The interval between stages in the other patients was 9, 5, 3, and 3 days, respectively. In all 5 patients the lobe was exteriorized at the second stage. In all of these patients, the pleural reaction was relatively unsatisfactory and the undiseased lobe was usually only loosely adherent to the parietal pleura.

The next main phase in the development of the operation was the gentle stroking of the pleuræ and elongation of the interval between stages to from 9 to 12 days. This has proved very satisfactory and there has been no death among the 6 patients operated upon (between April, 1930, and April, 1932) according to this procedure. I shall use in the future such minor modifications of it as have already been considered.

Several other lobectomies have been performed during the period of evolution of the operation just considered but as they illustrate no difference in principle, but only minor modifications to suit particular cases, I shall not discuss them, except to mention the results.

RESULTS

I have personally performed (between January, 1928, and April, 1932) 18 total lobectomies; 3 of the patients (16.66 per cent) have died. Only 12 (each with a non-adherent undiseased lobe) of these 18 have been operated upon according to principles that have been considered in the body of this article and 2 (16.66 per cent) of these have died (Table I). Six of these 12 have received the benefits of the developed technique and none of them has died.

All of the 12 patients suffered from clinically severe basal bronchiectasis and details of their cases are given in Table I. Four of them are cured

TABLE I.—TOTAL LOBECTOMY IN TWO STAGES FOR LOWER LOBE BRONCHIECTASIS

In all cases undiseased lobe was not adherent before operation

Number	Age at admission	Duration of disease	Before lobectomy							After lobectomy				
			Sputum				Cough colds pneumonia	Dyspnœa	Complications	Months between lobectomy and this report	Sputum			
			Amount in grams	Odor	Character	Streaking or hæmoptysis					Amount in grams	Odor	Character	Streaking or hæmoptysis
1	16	4 years	360	Fetid	Purulent	0	—	0	Otitis media	36	0	—	—	0
2	6	2 years	14–45	—	—	—	Pertussis	—	— —	1	—	—	—	—
3	18	15 years	120–140	0	Purulent	0	—	—	Maxillary sinusitis	31	65–80	0	Purulent	Occasional streaking
4	5	3¼ years	150–200	Foul	Purulent	One severe hæmoptysis and often streaked	Pneumonia and empyema	—	Otitis media	32	0–5	0	—	0
5	13	7 months	50–100	—	Purulent	Streaking	Non-resolution of pneumonia	Slight	— —	28	0	—	—	0
6	36	14 years	120	Foul	Purulent	More than 40 severe hæmoptyses	Abscess ?	Severe	0	0	—	—	—	—
7	37	4 years	72–220	0	Purulent	Frequent hæmoptyses 30 to 240 c.cm.	—	Severe	Pyelitis, pan-sinusitis, otitis media	25	0.5	0	Mucoid	Occasional hæmoptysis
8	14	7 years	100–240	Foul	Purulent	—	Pulmonary abscess	Severe	Toxic psychosis, pan-sinusitis	15	0	0	—	0
9	10	9 years	20–30	Occasionally foul	Purulent	0	Five attacks of pneumonia	Some	— —	29	16	0	"Green phlegm"	0
10	9	3 years	100–120	Foul	Purulent	Streaking	Severe cough, no pneumonia	Severe	Chronic otitis media, mastoiditis, and pan-sinusitis	9	4–10	0	Purulent	0
11	16	9 years	Up to 400	Foul	Purulent	Streaking	Five attacks of pneumonia. Severe cough	Severe	0	5	0	—	—	0
12	22	12 years	Up to 700	Foul	Purulent	Streaking	Pneumonia. Severe cough	0	— —	2	0	0	—	0

TABLE I.—TOTAL LOBECTOMY IN TWO STAGES FOR LOWER LOBE BRONCHIECTASIS (Continued)

In all cases undiseased lobe was not adherent before operation

TABLE I.—TOTAL LOBECTOMY IN TWO STAGES FOR LOWER LOBE BRONCHIECTASIS (Continued)
In all cases undiseased lobe was not adherent before operation

Number	After lobectomy									Remarks
	Cough colds pneumonia	Dyspnœa	Complications	Bronchial fistula: Open	Bronchial fistula: Closed and wound closed: Months after operation	Bronchial fistula: Closed and wound closed: How closed	No. of weeks in hospital	Gain in wt. (lbs.)	Present condition	
1	—	—	Considerable scoliosis	—	13½	Silver nitrate. Later, muscle plasty	20	20	Cured. Doing heavy labor with circus	Lobectomy 4-2-29 and 4-11-29
2	—	—	Œsophago-pleural perforation and peritonitis	[+]	—	—	18	—	Died 34 days after second stage	Average postoperative course and temperature-pulse practically normal 17th to 20th day. Then sudden sepsis and terminal œsophagopleural fistula and streptococcus hæmolyticus peritonitis
3	Colds	Slight	—	3x1x2 cm. opening	—	Thiersch grafts	11	8	Improved. Housework all day	Present sputum apparently from sinus tract distal to bronchial stump and from infected sinuses. Works 12 hours a day at house and farm work
4	Cough	—	0	—	20	Silver nitrate	13	10½	Clinically cured (but see Remarks). Regularly at school	There remains a dry bronchiectasis of the upper lobe on basal lobectomy side
5	—	—	Pneumonia, opposite lung. Severe scoliosis	—	11	Muscle plasty	16	37	Cured. At school and works in office or does chores on farm afterward	Wearing brace for scoliosis
6	—	—	Drowsiness and probable mediastinal emphysema	[+]	—	—	1½	—	Died 46 hours after unwise and partially successful attempt to free lobe from firm adhesions	Only moderate drop of blood pressure and rise of pulse first 36 hours. Drowsiness and difficulty in raising sputum were prominent
7	Moderate cough	0	Pulmonary tuberculosis	Occasionally open and slight discharge	—	Silver nitrate. Usually closed	17	12	Greatly improved	Five months after lobectomy a few early tubercles seen in roentgenogram and tubercle bacilli found at only one examination. Twenty-three months after operation coughed up head of a small gold safety pin
8	Slight cough	0	—	+	14	Spontaneously	10	31	Greatly improved	Toxic psychosis disappeared after lobectomy. Questionable bronchiectasis in contralateral lingula. Bronchial fistula reopened 15 months after operation, with associated moderate hæmoptyses
9	Occasional cough	0	—	—	7½	Spontaneously	14½	3¾	Greatly improved. Parents say, "As healthy as any boy." Regularly at school	There remains a practically dry bronchiectasis of the upper lobe on basal lobectomy side
10	0	0	Chronic otitis media, mastoiditis, and pan-sinusitis	—	2½	Silver nitrate	12	6½	Greatly improved	Chronic infection in ears, sinuses and mastoid remains as does a practically dry bronchiectasis of the upper lobe on basal lobectomy side
11	0	0	Acute hæmorrhagic nephritis	—	4½	Silver nitrate	24½	31	Cured	All symptoms of nephritis, including abnormal findings in urine and blood, disappeared about two months after lobectomy
12	0	0	Upper thoracic empyema, drained. Pyelitis	—	—	—	12	—	Operation too recent for classification as to result. Good prospect for cure	Empyema is now small. No signs of pyelitis

(see, however, Case 4); 4 are greatly improved and approximate a condition of cure; 1 is moderately improved; none is unchanged or worse, 2 are dead. One has been operated upon too recently for the result to be judged. By excluding this patient, 9 (81.81 per cent) of the 11 whose results are known are either cured or improved; 6 of the 9 have solidly healed wounds without a bronchial fistula and have little or no sputum. Consideration of the 2 deaths in retrospect leads me to believe that 1 of them (Case 2, Table I) was unavoidable and that the other (Case 6) was due to an unwise attempt to free a lobe from tough investing adhesions.

Six other lobectomy patients were operated upon by me (excluding 2 patients, 1 with carcinoma, the other with progressive multiple and already drained abscesses, operated upon with fatal result by other members of my staff) by techniques that are not directly related to the technique that is the subject of this article. The Whittemore operation, with the modification of tightly ligating the hilum close to the pericardium before exteriorizing the lobe, was used for 2, with 1 operative death and 1 cure. The Evarts Graham technique was used in many stages for a total lobectomy in 2 patients with dense pleural adhesions; 1 is without symptoms and his bronchial fistulæ have been closed with a muscle plasty and the other is slightly improved but has bronchiectasis of the upper lobe which is apparently uninfluenced by a very extensive thoracoplasty. One patient had a gigantic abscess and the other multiple abscesses, almost the entire lobe being involved in each case. The abscesses had been drained in both patients before lobectomy which was performed by interpleural isolation of the lobe and ligation of the hilum. One is cured and the other has no sputum but has been operated upon too recently for closure of his bronchial fistulæ.

Sixteen of the total 18 patients fulfilled the criteria that I believe necessary for safety in that they either had extensive adhesions over the undiseased lobe or they were caused to form before lobectomy was performed. Two (12.5 per cent) of these 16 died, 1 of them after an unwise attempt to separate adhesions before the lobectomy stage itself was undertaken.

Few operations require for a successful result such meticulous attention to pre-operative, operative, and postoperative details as does lobectomy.

OTHER METHODS

Almost every imaginable way of performing a lobectomy has been proposed or tried. The important methods have been described in a recent article by Ballon, Singer, and Graham, to which the reader is referred as well as to the original articles of the surgeons whose operations will now be considered. I shall limit myself here to a brief discussion of the principal types of operation.

The most fundamentally important difference of opinion exists today between those who favor one stage and those who favor two or more stage lobectomy. Many of the early lobectomies were performed in one stage. Lilienthal, a pioneer in lobectomy, reported in 1925 the largest series of one lobe lobectomies in one stage; there were 10 deaths (58.8 per cent) in 17 patients. There were 3 deaths in 5 two stage one lobe lobectomies and at that time Lilienthal preferred the one stage operation but used a two stage operation if the patient's condition was too poor to withstand completion of the operation in one stage. In a personal communication of May 6, 1932, to Ballon, Singer, and Graham, reporting what is presumably his entire experience with lobectomy for bronchiectasis (42 cases with 27 deaths) (64.3 per cent), Lilienthal announces his preference for a two stage procedure in which he rubs the pleuræ with gauze dipped in tincture of iodine and, at the second stage, resects the lobe, anchors the ligatures to the thoracic wall, separately ligates the vessels, and closes the chest except for a water-seal drain. Sauerbruch (31), in 1927, stated that he had had 6 deaths in 6 one stage lobectomies.

The high mortality figures of one stage operations and also of the two or more stage operations of only a very few years ago resulted in great pessimism about the propriety of employing lobectomy at all and this pessimism is evident in most of the present medical and surgical textbooks. In 1927, however, Whittemore reported 5 cases with only 1 death, operated upon by a one stage exteriorization technique that justly aroused interest and hope. This operation has been discussed elsewhere in this article. Brunn, in 1929, reported 6 cases with 1 death, operated upon by a one stage technique that was modeled after that of Lilienthal and of Garrè. Shenstone and Janes, operating in one stage, used an instrument with a cord snare that firmly squeezed the hilum without devitalizing it, while the lobe was being amputated and the stump closed carefully in layers, the last layer effecting pleura-to-pleura apposition and finally the stump was sutured to the under surface of the upper lobe. These features of the operation caused healing of the stump without bronchial fistula in the majority of cases. With this technique Shenstone and Janes lost only 2 of their first 13 patients and Archibald and Bethune 1 of their first 6.

udged by the critical standard of mortality percentage, the figures given in the preceding paragraphs renewed hope in lobectomy as a reasonably safe operation but the latest available reports of these surgeons are far less encouraging. Whittemore (37) has lost 3 of 10 patients, Brunn (10) 2 of . Shenstone and Janes (34) 5 of 16, Archibald (4) and Bethune 2 of 9 and three other thoracic surgeons who I have heard have used the Shenstone technique[1] have lost 2 of 3 patients. The combined figures of these cases, exclusive of the last 3, are 12 deaths (27.9 per cent) in 43 patients.

None of Shenstone's and Janes' patients died from hæmorrhage from the hilar stump, tension pneumothorax, pleural or mediastinal infection, one or the other of which has been responsible for 2 deaths following the Shenstone operation in another clinic and for many deaths after operations performed according to other one stage techniques.

There can be no question but that a one stage lobectomy through an intercostal incision with first intention union of the incision and of the lobar stump, and with only a temporary air-tight intrathoracic drainage tube, has obviously great advantages over any other technique that has been conceived and is a surgical ideal. But if in theory and practice a one stage lobectomy is considerably less safe for the patient than a two stage lobectomy, the ideal must be sacrificed. The best of the one stage figures to date are distinctly inferior to the best of the two or more stage figures.

Theoretically, any one stage operation, especially in the presence of a non-adherent undiseased lobe seems to me as dangerous as the figures indicate. A one stage operation takes much longer to perform than a two stage operation and for various valid reasons the time factor in a major operation, within a wide open pleural cavity upon patients so ill with grave suppurative pulmonary disease as to require a lobectomy, probably has considerable bearing upon the occurrence of postoperative pneumonia which has been a prominent cause of death in the one stage reports. I am told that the Shenstone operation takes about 1½ hours, though it has been performed in 45 minutes. It appears to me that in the long run pneumonia will not be combated more effectively by occluding the stem bronchus on the diseased side with various balloon devices than by the simpler measures that have been considered in this article.

One of the greatest theoretical as well as actual dangers of any one stage operation is that of infection of the pleura, mediastinum, blood, and thoracic wall. The intrabronchial secretions of these bronchiectatic lungs are loaded with highly virulent aerobic and anaerobic organisms. When the lobe is resected some contamination of the pleura in the neighborhood of the hilum from the opened bronchus is almost inevitable, in spite of careful protective packing. Although obliteration of the entire open pleural cavity, which Shenstone's technique tends to accomplish shortly after operation, does much to prevent the development of infection, it does occur not rarely. A virulent infection of an unprepared virgin pleura is certainly a grave complication, as is progressive infection within the already infected hilar stump which has been closed by suture in layers. This infection may not only quickly reach the mediastinal areolar tissue (Archibald, 4) but it may break down the catgut sutures that were used to close the bronchus and pulmonary vessels and break down the new thrombi with resulting secondary hæmorrhage (Archibald, 4) and bacteriæmia (Archibald, 4). Opening of the bronchus may cause fatal tension pneumothorax if the pleural drainage tube has become occluded by blood (Brunn, 8) or expanded upper lobe. If a patient is given large doses of opiates to help to keep him from coughing open the sutured bronchus, the danger of stasis pneumonia is greatly increased.

If the thoracic wall incision becomes infected and breaks open before the mediastinum has had time to become stiffened or the upper lobe to become firmly adherent to the costal pleura, the patient is exposed to grave danger of death from "mediastinal flutter" or its complicating pneumonia. Lilienthal (18) has warned against the danger of anaerobic infection of the thoracic wall incision (whose tissue spaces have not been sealed by a preliminary operation). A further danger of the Shenstone operation is that the temporary snare around the lobar stump may slip before the great pulmonary vessels have been closed by suture; this occurred in one of Archibald's (3) cases but the hæmorrhage was controlled before a dangerous amount of blood had been lost. The increased liability to brain abscess after primary lobar resection has already been discussed.

The evidence that is now available seems to me to dictate the conclusion that the margin of safety is far narrower with a one stage than a two stage operation. Consideration of one stage lobectomy should not be concluded without mention of the delicate and successful technique that Churchill (12) used in removing a carcinoma of the stem bronchus together with two pulmonary lobes and which will shortly be described by him. Churchill (11) prefers a two stage operation, preceded by temporary phrenic nerve interruption, for non-

[1] Tudor Edwards, in a recent letter, advises us that he has lost only 1 of 11 patients operated on by the Shenstone technique.

malignant pulmonary suppuration if the pleuræ are non-adherent. He has performed six lobectomies for bronchiectasis without a death, surely a remarkable record. One of his three lobectomy patients for carcinoma is well and two died.

To Samuel Robinson (23, 24) should go the honor of being the first to see clearly the important advantages of obtaining adhesions of the undiseased lobe before undertaking the lobectomy itself. It was because his various methods of producing these adhesions just missed being sufficiently effective that lobectomy was not accepted as a useful operation 15 years ago. In his last clinical report he (26) stated that, if it were only possible to get the undiseased lobe anchored and to remain anchored, the chief obstacle to successful lobectomy would be removed.

Sauerbruch has apparently been frequently dissatisfied with the techniques he has used and has often changed them. At first (28) he used a one stage operation; then (28) a "piece-by-piece" (stueckweise) lobectomy; then (28) ligation of the lobar artery and removal of the lobe at a second stage; then in 1928 (32) presumably in stages, phrenicectomy, thoracoplasty, ligation of the lobar artery, and if it were possible to free the lobe to the hilum, resection and separate ligation of the artery and vein when feasible, but mass ligation when the hilum was especially tough. In weak patients and apparently for others, he advised instead of this procedure, removal of a few ribs and an extrapleural pneumolysis with paraffin filling and 6 to 8 weeks later an extensive thoracoplasty with the paraffin in place and, 3 to 4 weeks later, removal of the paraffin and of the lobe as the final stage. He also wrote at this same time (1928) of having used an extensive thoracoplasty and later, after separating the lobe from adhesions, packing gauze around it and repeating the packing and pressure and, finally, tearing the lobe free from its adhesions and ligating its hilum with a rubber tube (Zaaijer, 38, 39). Nissen, in 1929, writing from the Sauerbruch Clinic, advised using an elastic hilar ligature (Lenhartz) if the hilum were not well fixed in dense scar, and if it were, he advised resecting between mass ligatures. Nissen, in 1930, described in some detail the use of paraffin either extrapleurally or intrapleurally when some pleural adhesions already exist, in an effort to produce pleural adhesions as well as to compress the diseased lobe. He advised 2 week intervals between the first and the second, and the second and third stages instead of the much longer intervals that Sauerbruch had recommended 2 years before. Nissen at that time proposed surrounding a non-adherent diseased lobe with a cloth bag (Robinson, in 1917, surrounded it with a gauze pack). The last report from the Sauerbruch Clinic came from Nissen in 1931, emphasizing the importance of having adhesions all the way to the hilum and advising repeated packing before removal of the lobe with an elastic ligature, but it is difficult to tell from this article whether or not Sauerbruch has as yet entirely lost his faith in the ability of extrapleural paraffin to form sufficiently extensive pleural adhesions to make lobectomy safe. Denk, in 1929, observed that extrapleural paraffin, placed over the diseased lobe as Sauerbruch places it, does not cause formation of adequate adhesions over the undiseased lobe, and I do not understand how it could be expected to cause the desired reaction in the mediastinal and hilar pleura.

It appears to me that the Sauerbruch techniques are unnecessarily complicated, that what seem to me as unnecessary major operations (stages) increase the patients' jeopardy, and that in none of them is any direct effort made to create firm adhesions over the undiseased lobe. These same criticisms apply to the technique employed by Zaaijer and Coryllos. It is not made clear by Sauerbruch, whether or not he has included in his reported statistics any deaths that may have occurred during the thoracoplasty and other stages preliminary to the lobectomy stage proper. If I should not count the death that occurred in Case 6 of Table I after the operation that was performed 10 days before the intended lobectomy, my mortality would be 1 death in 11 cases or only 9.1 per cent instead of the 16.6 per cent that I consider the correct figure for the series about which the article is primarily written. I recognize that in a narrow sense, a statistical report on "lobectomy" might be considered to include only those patients upon whom lobectomy was actually accomplished, but on the other hand, any death occurring after any stage whatever that the surgeon considers to be a necessary preliminary to the lobectomy itself should properly be counted as a lobectomy death.

The following reports of two or more stage lobectomy (but usually without clear indication as to what techniques were used) have been made from the Sauerbruch Clinic (exclusive of the "piece-by-piece" lobectomies in which there were 2 deaths in 9 patients): 1920, 6 lobectomies, 0 deaths; 1924, 10 lobectomies, 3 deaths; 1929 (30), 23 lobectomies, 3 deaths and "all the others were cured, not only improved"; 1928, 26 lobectomies, 3 deaths; 1929 (Krampf), 28 lobectomies, 3 deaths; 1931 (Nissen), 38 lobectomies, 4 deaths. These are indeed phenomenal figures and especially startling is the apparent claim that there was but death

in years among 28 patients (compare the 1924 and the 1931 figures just given). Also startling is Sauerbruch's bald 1927 statement that every one of the 20 patients who have survived the operation is actually cured, by which should be understood a solidly healed wound without any bronchial fistula whatever, and 5 grams or less sputum in 24 hours. When, however, Sauerbruch's one stage and piece-by-piece lobectomy cases are added to his two or more stage lobectomy cases, there is a total of 53 cases with 12 deaths, a mortality rate of 22.6 per cent.

SUMMARY

1. The many dangers inherent in resection of an entire lobe of the lung are expressed in the prohibitive mortality rate of 53.4 per cent for 127 collected cases in which recent improvements in technique were not applied.

2. Another series of 115 cases has been collected from the 8 foreign and native clinics which have contributed most to the study of lobectomy, with a mortality rate of 21.5 per cent.

3. In this article are reported 18 personal cases with 3 deaths, a mortality rate of 16.6 per cent. None of the last 8 has died.

4. The undiseased lobes of 12 of these 18 patients were not adherent and special measures were taken to overcome this particular danger. Two died (16.6 per cent). Only 6 of these 12 patients have received the benefits of the developed technique and none of them has died.

5. The principles of the operation and its technical details are given.

6. The other modern lobectomy operations are critically considered.

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INTRAVENOUS PYELOGRAPHY

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ONLY a short time has elapsed since the fundamental researches of Roseno, von Lichtenberg, Swick, Binz, Lichtwitz, and Hecht first made it possible to obtain adequate radiographic demonstration of the urinary tract by means of an intravenously injected contrast agent. Nevertheless, a large number of important papers have already been published which have led to the rapid development and exploitation of this valuable diagnostic method. Haenisch recently gave a comprehensive review of the scope and application of the method at the International Radiological Congress in Paris, and at the same time summarized the history of its discovery. Anyone wishing to obtain a clear outline of the development of the method from unsatisfactory beginnings into a valuable addition to our diagnostic armamentarium, should not fail to consult Haenisch's article.

It is unnecessary to recapitulate here the steps in the development of the method, since Haenisch has traced this in its entirety up to and including the introduction of the newest contrast medium for intravenous pyelography, uroselectan B, though the element of time has prevented him from reporting upon any very extensive experiences. In contradistinction to Haenisch, we incline to the opinion that to a certain extent uroselectan B, represents a final stage in the development of intravenous pyelography. Not only has the reduction of the amount of solvent to 20 cubic centimeters greatly simplified the application of the method but in addition the excretion of iodine in the urine has attained a perfectly adequate concentration for contrast purposes and further, under ordinary circumstances, it is limited to a short period of time.

Uroselectan B is a pyridin derivative with 51.5 per cent of organically combined iodine. Twenty cubic centimeters contain 15 grams of the substance dissolved in a 10 per cent solution of invert sugar. This amount is sufficient to give clear pictures not only of the urinary tract but also of the renal parenchyma. Although the solution is hypertonic, the addition of invert sugar has, according to our experience, prevented the appearance of such symptoms as a sensation of warmth, thirst, perspiration, nausea or vomiting; we have not observed such effects after the injection of uroselectan B. Occasionally the patients complain of a drawing pain along the veins in the upper arm, radiating into the forearm. These pains are a sign that the injection has been carried out too quickly and can be avoided by injecting more slowly. They are not the precursors of thrombosis, a phenomenon which we have not observed in any case.

Since uroselectan B does not influence the coagulation time or sedimentation rate (von Lichtenberg), there need be no fear of the occurrence of thrombosis or embolism, provided the technique of injection is correct. According to Haenisch, uroselectan B may be used in all conditions with the exception of uræmia, and our experience confirms this view. Analysis of the urine (Heckenbach) shows that in the first hour following the injection (especially the first 10 to 50 minutes) uroselectan B is excreted almost quantitatively; there is a marked diuresis and the urine shows a high percentage of iodine (about 5 per cent). This property is responsible for the relatively good contrast of the films obtained and for the fact that the ureters are more often filled throughout their whole extent than is the case with other contrast agents. This observation is of particular importance, as previously individual authors have considered the demonstration of the ureters in their whole extent as a sign of a pathological condition or irregular function. In spite of all its obvious advantages, we must entirely agree with Haenisch's statement that intravenous pyelograms also are upon occasion useless. This is due to the fact that the pictures are relatively weaker in contrast than those obtained with retrograde pyelography. While practice gradually enables the eye to interpret the meaning of the pictures, it sometimes happens that the amount of gas or fæces in the gut seriously interferes with the demonstration. Many methods are adopted to avoid this and we have gained the impression that, in ambulant and unprepared patients, this phenomenon is least frequently and less markedly observed. Nevertheless, it is not possible to exclude such an occurrence with absolute certainty and under such circumstances the demonstration of the renal pelvis by means of retrograde pyelography will give better results.

Furthermore, retrograde pyelography remains valid not alone for such cases. Plaumer has recently pointed out that the basis of intravenous

pyelography, and, therefore, its indications are entirely different from those of retrograde pyelography. With the latter method we are dealing exclusively with the demonstration of a normal or pathological condition of the *lumen* of the urinary tract. In this connection, it must not be forgotten that if the contrast agent is instilled at a pressure higher than the normal for the urinary tract, an artificial and deceptive dilatation may take place and an accurate picture of the size of the renal pelvis is not necessarily obtained. The intravenous method, while it demonstrates gross changes in the anatomical condition, also gives us information as to the size and shape of the renal parenchyma and of its functional activity. This fact enhances the value of the intravenous method from the point of view of diagnosis. From the technical standpoint, the intravenous injection of 20 cubic centimeters of uroselectan B is far more agreeable for the patient than ureteric catheterization. It follows, therefore, that the intravenous method with its superior adaptation to physiological conditions, should, in most cases, precede the application of the retrograde method, the employment of the latter being only necessary when the information given by the former proves insufficient.

In accordance with the observations of Heckenbach on the rate of excretion of uroselectan B, the X-ray exposures are best made within a period of 10 to 50 minutes after the injection. In some of our cases excellent pictures of the renal pelvis were obtained 6 minutes after the completion of the injection, this having been carried out with the patient lying on the X-ray table (Fig. 1). Occasionally, the most strongly contrasting pictures were obtained by taking a series of films at intervals of 10 minutes up to 90 minutes after the injection. Perlmann refers to the fact that previous investigation of the rate of excretion of indigocarmine may give some indication of the best time for making the exposure. When the kidney function is damaged, the excretion of the contrast agent may be delayed on one or both sides, and the X-ray investigation may have to be prolonged even into the next day, the exposures being made at longer intervals, before a complete picture is obtained. The pictures gain in definition when the contrast agent is held up in the renal pelvis by means of compression. We were not able to convince ourselves that pressure over the bladder region was of much importance for the success of the pyelogram. It is far more effective to constrict the ureters at the level of the sacrum (Ziegler, Koehler, etc.); in any case pressure should not be applied until urine containing the contrast agent has collected in the renal pelvis. If the compressor is applied too soon, urine containing the contrast agent will become mixed with urine free from it and the contrast in the X-ray plate will suffer. With the use of compression, the middle section of the ureter remains unfilled and is not, therefore, demonstrable. This condition must not be confused with occlusion of the ureter due to stone, etc. Further, if the renal pelvis appears large, there is no reliable method of knowing whether this is due to the stasis produced by the compression or not. For this reason we loosen the compressor as soon as a sufficiently good picture of the renal pelvis for diagnosis has been obtained. In spite of all precautions, however, it is not always possible to demonstrate the urinary passages in their entirety. Slight changes in the contours of the renal pelvis in particular (small, shadowless stones, small tumors, tuberculosis, etc.) are sometimes better demonstrated by ascending (retrograde) pyelography.

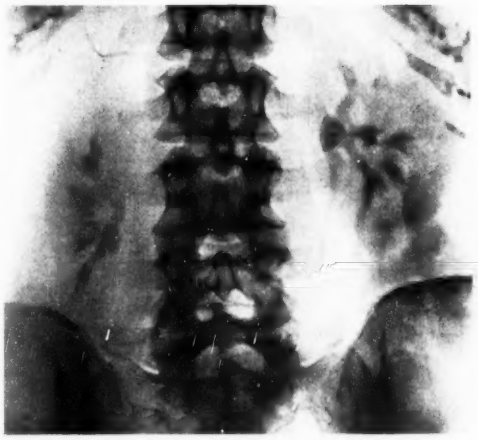

Fig. 1. Taken immediately after injection. Position of right kidney low, normal pelvis. On the left, renal pelvis is double and two small kidney shadows are seen which in combination give rise to a renal contour somewhat similar to the normal.

In view of the complexity of the subject and in order to be as concise as possible we would once again refer the reader to Haenisch's paper for a description of various individual points and of the normal appearances. We will confine ourselves here to the discussion of various important points as they arise in the course of describing some especially typical cases.

Figure 1 was obtained immediately after the injection. The left renal pelvis is double. The pelvis can be well seen even to the finest details of the

Fig. 2. Forty-five minutes after the injection. Concentric enlargement of the right renal pelvis which has a prolongation, similar to the root of a radish, opening into the ureter. The left kidney shows no excretion and no shadow of the parenchyma. The bladder is empty. Diagnosis: left kidney not functioning on account of destruction of the parenchyma from the hydronephrosis. Intermittent hydronephrosis of right kidney (see text).

calyces. In the lateral renal pelvis practically only the calyces are filled and the anatomical pelvis shows only a thin contrast shadow. Such pictures often alternate with others in which the same renal pelvis is completely filled and clearly demonstrable. The phenomenon is especially noticeable in small sized renal pelves, and we attribute it to transient contractions (Manges, Haenisch). In this case, however, another possibility must be considered. The parenchyma corresponding to both renal pelves is markedly penetrated by the contrast solution and is, therefore, clearly visible. The parenchyma shows the appearance of a double kidney and both parts are nearly reniform. The lateral portion of the parenchyma is the smaller in relation to the size of the pelves. The larger portion of the double kidney to which the medially placed pelvis belongs, lies with its most voluminous part corresponding at every point exactly with the position of the anatomical renal pelvis in the lateral section of the kidney. These topographical relationships suggest that possibly the laterally placed renal pelvis is developed only as a narrow fissure and that as a result the thin layer of contrast urine lying in it is not sufficient to demonstrate the pelvis. This possibility must be the more seriously considered since in subsequent exposures no improvement was seen in the demonstration of the renal pelvis. The appearance is not therefore due to transitory contractions but to a permanent condition. Still more the excretion of the contrast urine on this side was practically complete at the end of 30 minutes after the injection. In the pyelogram obtained at this time, the renal parenchyma showed the normal degree of opacity to X-rays, from which it may also be assumed that the excretion of contrast urine on this side has come to an end. For the same reason it is no longer possible in the last exposures to differentiate between the two sections of parenchyma of the double kidney.

To this must be added the fact that even 10 minutes after the completion of the injection, the parenchyma and pelvis of the left side show only very weak shadows. On the other hand, the parenchyma of the right kidney was unusually clearly visible during the whole time of observation up to the end of 30 minutes, that is to say it was heavily filled with contrast agent. Here too contrast urine was present in the pelvis immediately after the injection. The best degree of filling was obtained 10 minutes after injection but also after 30 minutes the renal pelvis was as easily demonstrable as immediately after the injection. Only after 30 minutes did the pictures gradually become less dense. It cannot be said with certainty whether or not these chronological differences in excretion are due to the obvious congenital malformation of the left kidney. Such greater differences in the excretion time are described by Haenisch; in such cases, however, pathological changes are undoubtedly present. But in this case also it is particularly worthy of notice that not so much the excretion but the accumulation of the contrast agent in the parenchyma, first sets in on one side long after the

Fig. 3. Thirty minutes after injection. Normal pyelogram on left side. On the right side moderate dilatation of the renal pelvis with flattened out calyces. The ureter is slightly dilated as far down as the sacral region. In its neighborhood traces of contrast agent used for the demonstration of an abscess fistula are to be seen. Diagnosis: hydronephrosis due to involvement of the ureter in adhesions resulting from a retrocolic abscess due to an attack of appendicitis during pregnancy.

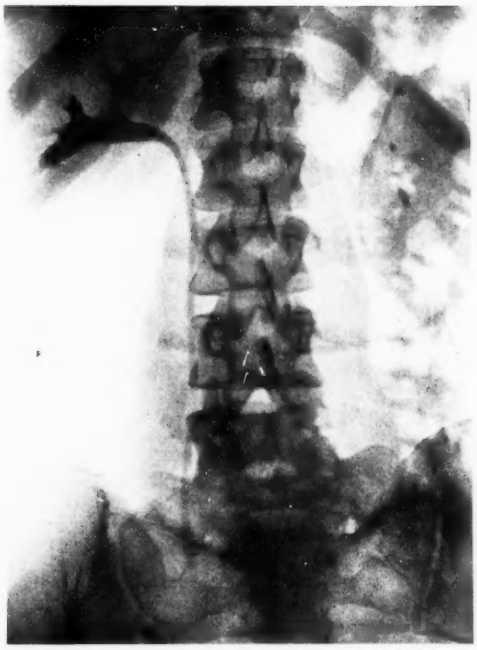

Fig. 4. Twenty minutes after injection. The right kidney is displaced upward and is somewhat compressed. The neck of the renal pelvis, which is normally directed downward, is turned inward, and the ureter filled with contrast urine runs downward along the right border of the vertebral column. While the excretion of contrast urine has passed its maximum point on the left side, on the right side the intensity of the shadow remains the same. One can see "tufts" which are due to filling of the renal tubules with contrast urine, and which appear as continuations of the ends of the calyces. The renal parenchyma is completely intact. Diagnosis: retroperitoneal lipoma.

maximum point of excretion has been reached on the other side. Sufficient observations have not as yet been made to enable one to say how far small chronological differences in the penetration of the contrast agent into the parenchyma and its excretion into the renal pelvis are physiological or otherwise. It cannot, therefore, be decided with certainty whether the above described functional condition is pathological. An important point, however, is the fact that the accumulation of uroselectan B in the renal parenchyma can take place at different times in the two kidneys. Further it can be clearly shown that unilateral anuria due to prerenal causes, does not lead to such a degree of compensatory activity in the other kidney as to permit the latter to excrete the whole of the contrast agent, but rather should it be said that the first kidney can later make up for its deficient activity. For this reason the process of excretion must be observed if necessary over a prolonged period.

Figure 2 is a reproduction of one of the pictures obtained from a case in which such considerations as mentioned were of clinical significance. The pelvis of the right kidney is greatly enlarged and presents flattened contours on all sides. The cusps of the calyces are also enlarged and flattened out. The renal pelvis runs downward sharply and irregularly like the end of a radish, which is strongly suggestive of a constriction of the ureter at this point. The exposure was made 45 minutes after the injection and is in the main similar to its predecessors. The accumulation of the contrast agent in the kidney parenchyma cannot be demonstrated since it is obscured by a collection of gas in the colon. None of the films showed the presence of contrast urine in the bladder. Only after hours of delay was the contrast fluid evacuated from the renal pelvis. This observation definitely shows the presence of an intermittent hydronephrosis. Since the ureters cannot

Fig. 5A. 20 minutes after injection. Both renal pelves are filled with contrast urine, the right being lower than the left. The right renal pelvis is much nearer the middle line than normal so that its two lower calyces which are almost vertical lie immediately above the lateral process of the fifth lumbar vertebra. Shadow of the renal parenchyma poor on both sides. Probable diagnosis, horseshoe kidney.

be demonstrated in all cases, this diagnosis can obviously be made only when contrast urine consistently fails to fill the bladder, that is to say when the other kidney excretes no urine into it as happened in the case under consideration. We were able to observe this case uninterruptedly for only 9 hours after the injection and 24 hours after the injection we made another control exposure with exactly the same result. At no time in the course of the examination was contrast urine found in the left kidney or ureter.

Such findings can be correctly interpreted only in association with the general history of the disease and the results of other examinations.

A farmer, aged 49 years, complained of attacks of pain in the left upper abdomen and loin for the last 12 years. These have increased in frequency and of late have been accompanied by vomiting and constipation. The corresponding area is tender on examination and palpation. Intake and excretion of water maintained a balance during a period of a week. The specific gravity of the urine varied from 1018 to 1020. The test for albumin was positive. The sediment showed large numbers of erythrocytes and many leucocytes. No œdema was present. The patient excreted 375 cubic centimeters of urine 1 hour after taking 1,000 cubic centimeters of tea and after 2 hours 425 cubic centimeters of a specific gravity of 1003. On a dry diet the specific gravity of a small quantity of urine passed in the evening varied from 1017 to 1020. Methylene blue was excreted from the right ureter 5 minutes after injection and from the left in 9 minutes. The urine from the left ureter was only very faintly tinged with blue. Retrograde pyelography was not successful on the left side. On the right side, a pyelogram similar to that shown in Figure 4 was obtained. A review of the individual findings permitted the diagnosis of functional deficiency of the left kidney together with maintenance, or perhaps a compensatory increase of the functional activity of the right kidney. At operation the parenchyma of the left kidney was found to be almost completely destroyed. Behind the kidney, which was closely adherent to the surrounding structures, was a rigid walled renal pelvis. Its lumen was compressed to a small slit, from the lower lateral pole of which came the ureters. A few drops of cloudy urine could be expressed from it. Dilatation of the pelvic lumen was impossible on account of the rigidity of its walls.

Thus while retrograde pyelography could only show the anatomical changes of the right renal pelvis, intravenous pyelography showed that the kidney had preserved its functional activity. Absence of any contrast agent in the parenchyma of the left kidney justified the conclusion that the power of concentration of the left kidney for the given test substance, i.e. uroselectan B (Lichtwitz), was as deficient as for indigo and other dissolved substances. It could also be assumed that the unilateral functional deficiency was responsible for the observed disturbances in the fluid exchange. In this connection it must not be forgotten that there is always the possibility of reversible suppression of function, particularly in association with ureteric calculi.

In another case the establishment of the diagnosis was more simple (Fig. 3). In this patient a hydronephrosis had developed as a result of a retrocolic abscess following upon appendicitis during pregnancy, the right ureter having been involved in adhesions. In this case also the intense shadow produced by ascending (retrograde) pyelography, is characteristic. Hydronephroses due to mechanical obstruction are excellent cases from the technical standpoint for intravenous (descending) pyelography, since they cannot always be filled from below with the same degree of certainty. The question arises as to whether the increased contrast obtained is due to a greater concentration of iodine in the urine or to the fact that the X-rays have to pass through a thicker layer of contrast urine. This can be definitely decided only by estimating the decline

content of a specimen of urine removed through the ureteric catheter; from the intensity of the shadow of the ureters in our film, however, it is evident that no appreciable increase in the iodine content of the urine has occurred and that the increased contrast obtained is due rather to the thickness of the hydronephrotic sac and the thickness of the layer of contrast urine contained in it. The ureter is especially dilated in its iliolumbar portion. At the point where it passes into the small pelvis, the width of its lumen is normal. The seat of the constriction must therefore be searched for in the region of the sacro-iliac joint. This point was also indicated by investigation of the course of the abscess fistula with iodipin. (Traces of the iodipin are to be seen as fine flecks of metallic density from the neighborhood of the ilium up to the renal pelvis and ureter). On the opposite side the excretion of uroselectan B is normal.

A characteristic case for intravenous pyelography may be briefly referred to here. In a 23 year old household worker a solid tumor with a smooth upper surface was found filling the whole of the right abdomen. It had gradually grown to its present size and had displaced the ascending colon forward and toward the middle line. As is shown in Figure 4 there was a similar displacement of the right ureter. Other clinical signs contributed nothing to a more definite diagnosis.

After intravenous pyelography had been done the possibility that the tumor was connected with the kidney could be definitely excluded. This opinion was justified not only by the fact that no characteristic changes were found in the renal pelvis but far more because the renal parenchyma was filled with the contrast agent and its contours were on all sides well defined, and the mottling such as would have been present in the presence of a tumor was entirely absent. This fact was definitely demonstrable in all the films. Actually the condition was due to a retroperitoneal lipoma weighing 3 pounds. In this case also we observed a difference in the time of excretion of the contrast agent by the two kidneys. Figure 4 was taken 20 minutes after the injection. At this time the excretion of contrast urine on the left side was, as in Case 1, already on the decline. As a measure of this, we must consider not only the filling of the renal pelvis with contrast urine but also the intensity of contrast of the parenchyma. In a series of films it is easy to recognize the increase and decrease of intensity which correspond to the functional activity of parenchyma and renal pelvis.

In well contrasting pyelograms such as the present, the urinary tubules are not infrequently

Fig. 5B. Taken in oblique position showing left kidney pelvis. The pelvis and the upper part of the ureter form a curve concave posteriorly. The upper sections are placed more posteriorly than the lower. Probable diagnosis, horseshoe kidney.

demonstrable and give rise to the appearance of "tufts" which converge upon the ends of the calyces. These tufts are the same as those which, as is well known, are sometimes found after retrograde (ascending) pyelography. In comparison with the latter, however, the appearance obtained with intravenous pyelography is less distinct. Individual urinary tubules cannot be distinguished from their neighbors, a fact which supports the theory that the urinary tubules cannot be demonstrated by retrograde pyelography unless they are distended.

Intravenous pyelography was carried out in a 26 year old farmer who complained of trouble following a kick in the region of the right loin, sustained during the previous year. Ureteric catheterization could be carried out only on one side on account of the displacement of the mouths of the ureters. Figures 5A and B, which were obtained in this case, show that in addition to this anomaly of the ureter, the kidneys also had some peculiar features. The right kidney was more than one vertebra lower than normal and was partly displaced medially in front of the vertebral column. The left kidney lay obliquely. In order definitely to exclude the unlikely diagnosis of a floating and dropped kidney, an exposure was made in the upright position (vide Röfo), which showed no alteration in the position of the kidney. It should be pointed out in this connection that the taking of pyelograms in the vertical position which is necessary in some cases, has been greatly

simplified by intravenous pyelography. With the retrograde method the presence of a cystoscope and ureteric catheters makes this position very unpleasant for the patient unless special arrangements are made.

Unfortunately the parenchyma contained so little of the contrast agent that it was not possible to prove or exclude the presence of a horseshoe kidney, which seemed the most likely diagnosis. On the other hand both renal pelves were so well filled with contrast urine that by the combined use of a tube and a lead screen it was possible to obtain oblique views of them, one of which is reproduced in Figure 5B. The whole of the left renal pelvis can be clearly seen. The central beam of rays has illuminated the renal pelvis in the same plane as a typical longitudinal hemisection so that all the calyces together with the anatomical pelvis are projected in approximately the same plane. This appears to circle round the vertebral column in a slight curve resembling a flat spiral. The upper calyces lie more posteriorly, the lower more anteriorly; the pelvis is displaced in a similar way. The upper part of the ureter continued this curve and then, somewhat lower down it bends fairly sharply backward; this peculiar course speaks with some certainty for the presence of a horseshoe kidney.

As a supplement to the numerous earlier works on the same theme, these observations and examples will help to determine the limits and possibilities of the new method. It must be pointed out that not all pictures obtained by intravenous pyelography will lead to an exact diagnosis. It can, however, be said that the production of uroselectan B constitutes a considerable advance in increasing the reliability of the results.

IRRADIATION IN A CASE OF OSTEOGENIC SARCOMA; RECOVERY

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TWO report an isolated example of a pathological condition and the result of its treatment is usually without excuse. If, however, the pathological condition should be a malignant bone tumor and the treatment has resulted in cure then such a report becomes not only excusable but desirable. Furthermore, if the successful method has been one which has given few or no favorable results previously the case assumes even greater interest. It is proposed to describe the radiation treatment of a case of osteogenic sarcoma and the results obtained. A few general remarks on bone tumors are included.

There is a vast amount of misunderstanding of every aspect of both benign and malignant bone tumors. Much of this is traceable to the lack of a uniform precise terminology, as has been stated by others. The variability of development of the mesenchymatous tissues has refined pathological classification out of proportion to the essential basic differences to be found in the new-growths of bone. Causes which cannot be even surmised are operative in the metaplasia of the tissues of the connective tissue group. Bone, fibrous and myxomatous tissue cartilage, alone or in combination, mature or embryonic in type, may compose bone tumors. But, however made up, the origin is from the same primitive connective tissue type. If this fact is kept in mind the problem of bone tumors becomes simpler. The natural history of connective tissue and the tumors arising from it only become difficult to understand when too great an ingenuity is used to interpret it.

Contributing to the confused state of knowledge of bone tumors is, fortunately, their infrequent occurrence. Few physicians, except in the larger clinics or hospitals, have the opportunity for extended and intensive observation of these tumors. Coley quotes a British estimate of 400 osteogenic sarcomata in England in 1923. Codman is authority for the statement that in Massachusetts (1929) there was one case of bone sarcoma for each 100,000 of population.

The incidence of bone tumors in the group of hospitals allied to the Washington University School of Medicine has been 96 cases in 123,285 admissions in 18 years. The relative incidence of bone sarcoma to sarcoma of other tissues is 24:31. There have been 220 sarcomata of all types, 96 of which were skeletal.

In spite of the efforts of the Registry of Bone Sarcoma of the American College of Surgeons and the writings of Bloodgood, Kolodny, Ewing, Geschicter and Copeland, and others, an astonishing ignorance of malignant bone tumors and their nature persists.

A sharp distinction should be made between tumors that are osseous by virtue of their origin and those that are osseous because of location. The first of these are strictly osteogenic tumors. Osteogenic has been frequently pointed out as an unfortunate term as it is a prolific source of confusion. Its correct meaning designates the origin of bone tumors from osteoblastic tissue. Often, however, the word is used in a way to imply the *generation* of bone. As this phenomenon, i.e., the development of new formed bone, is encountered in a variety of conditions which are benign, some of them even being physiological or normal repair processes, it is of minimal diagnostic and prognostic value in the consideration of malignant bone tumors. Moreover, in osteogenic sarcoma of the most malignant type new bone formation may be entirely lacking throughout most of the course of the disease. Osteogenic sarcoma is, therefore, defined as a malignant bone tumor that arises from true bone tissue. They are to be separated from malignant tumors arising from the tissues

Fig. 1. Roentgenogram made February 2, 1922. Anteroposterior view of right knee joint. Lateral view made same date on glass plate which was broken and hence is not shown.

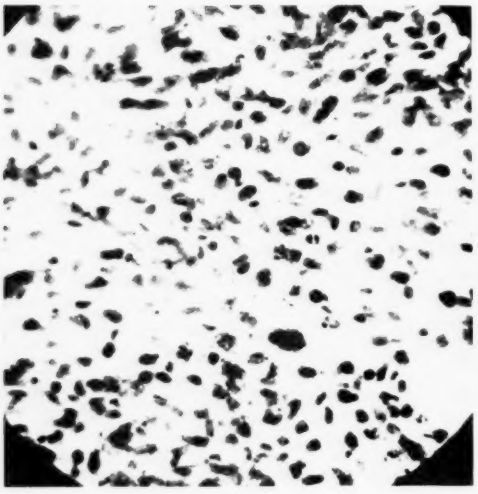

Fig. 2. Photomicrograph of section showing undifferentiated cell type.

Figs. 3 and 4. Photographs of leg made after exploration, March 13, 1932.

which invest bone or those which are housed in bone. In the former class are subperiosteal fibrosarcoma and capsular sarcoma, and, in the latter, endothelioma of bone (Ewing's tumor), the myelomata, angio-endotheliomata, and the epithelial tumors of the jaws of dental origin.

Giant cell tumor should be referred to here, but only because it is so often unfortunately designated giant cell sarcoma, this term implying malignant qualities. Indeed, especially when its treatment is being considered, giant cell tumor is often relegated to the same category as the malignant tumors that are found in bone. Thus arises much confusion as to methods and value of treatment. This disease is an independent pathological entity and its relationship to bone tumors is merely a matter of anatomical location.

The treatment of malignant bone tumors is by surgical removal, irradiation, and Coley's toxins, either singly or combined. The oldest and most widely employed method of treatment is surgical removal of the tumor by amputation in the case of the extremities, and by excision in the case of tumors of the axial skeleton. The latter is, of course, not always possible. At this point the limitations of the application of surgical treatment of osteogenic sarcoma appear.

The objective in the surgical treatment of osteogenic sarcoma is complete removal of the new-growth. Unless all of the tumor is removed recurrence will follow surgical attack. Success is more apt to follow surgical operation on the extremities than those of the trunk. The weak point in surgical operation is the fact that at the present time there is no way of determining the exact limits of the tumor. Some value in this direction attaches to exploration of the vessels and marrow cavity in the involved member and locating the field of operation at a point where these structures are free from tumor. It should be remembered that sarcomatous extensions follow the paths of least resistance. These are the interior of blood sinuses and vessels, the loose tissues of the marrow cavity and the loose areolar tissue of the fascial planes and intermuscular septa. Since this is written by a radiologist, these points, though well known, are reiterated for the purpose of emphasizing the fact that radiotherapy must be directed to the tissues and areas enumerated to the ultimate limit to which the tumor might possibly extend. The necessity of this is either not understood or is neglected in radiotherapeutic methods. The impossibility of determining the extent of sarcoma is the reason for the failure of both surgical and radiological treatment of this disease. There is an advantage in the toxin treatment of bone sarcoma as compared with either surgery or irradiation. It reaches the ultimate limit of the disease with certitude because the circulation is its vehicle. Determination of the tumor limits for surgical or irradiation treatment is necessarily based on a very crude estimate.

Figs. 5 and 6. Roentgenograms of March 10, 1922. Anteroposterior and lateral views of the tibia shortly after exploratory operation before irradiation.

Figs. 7 and 8. Roentgenograms of April 13, 1932. Anteroposterior and lateral views of tibia at the time deep X-ray therapy was instituted.

It has been stated that of the therapeutic methods employed in bone sarcoma, surgical removal is the oldest, the most widely used, and has resulted in the greatest number of recoveries. It is a more stabilized form of treatment and there is far greater unanimity of opinion as to the details of its application and the results obtainable than is the case with either the toxin or irradiation treatment of bone tumors.

The toxin treatment has not been as widely used as it deserves to be. One cannot read Coley's reports without drawing two conclusions. First, that in Coley's hands his toxin treatment has yielded more impressive results than can be found in any other method of treatment. Second, it should be more widely, skilfully and faithfully used than seems to be the case except in Coley's hands.

Of the three methods of treatment of osteogenic sarcoma, irradiation is the least understood and the most inconsistent in application and has the greatest diversity of opinions as to methods of use. This vagueness and uncertainty is due to the developmental state of radiotherapy. This is particularly true as regards X-radiation. Here there has been constant change of method, apparatus, and technique of administration. This has been so diverse that it is impossible for one to evaluate the results of treatment of a few years ago as compared with those of today. Fortunately, this is partly explained by the fact that there has been such great progress in the direction of greater efficiency of this agency. Even with radium there has been great variation in methods and views as to the application of this more stable agent. It may be added that there is no immediate prospect of the complete stabilization or standardization of radiotherapy.

There should be no therapeutic distinction between X-irradiation and radium irradiation on the basis of any particular specificity of ray for pathological tissue, though many authorities will dispute this statement. The object to be attained in irradiation is absorption of the correct amount of ray by the tumor tissue. This is at times achieved by radium and at others by the X-ray. Frequently it is advantageous to employ a combination of the two, for example, distance irradiation by X-ray following interstitial radium irradiation.

It is a deplorable fact that venal consideration sometimes determines the choice of the use of radium or X-ray.

Irradiation of osteogenic sarcoma has been chiefly applied to the far advanced cases or as an adjunct to other methods of treatment. In the latter class of cases it is chiefly used for recurrences and metastases. In short, it is applied to unpromising material.

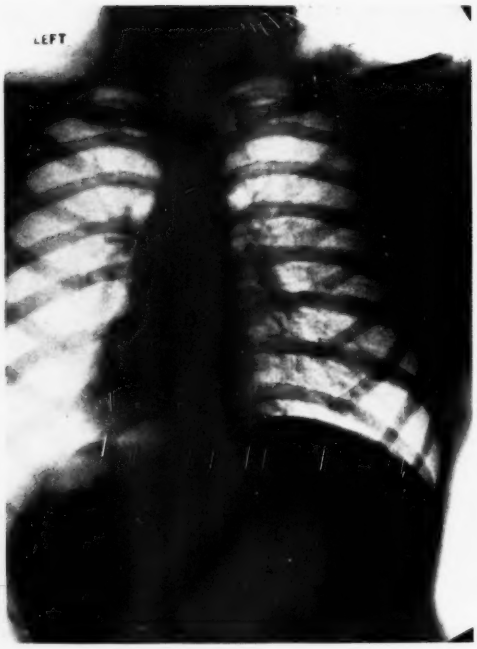

Fig. 9. Roentgenogram of chest made on June 1, 1922.

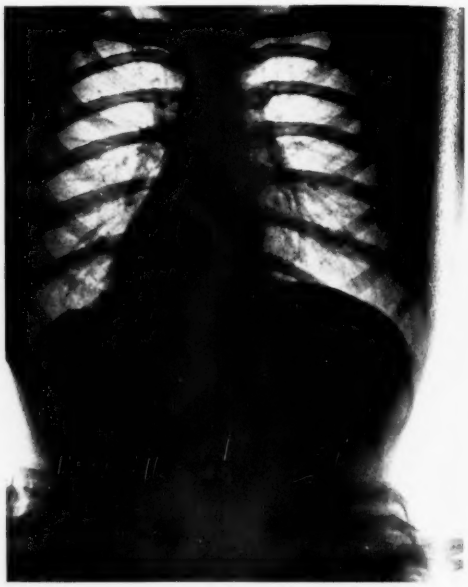

Fig. 10. Roentgenogram of chest made on July 23, 1932.

Ewing is authority for the following: "yet some cases of osteogenic sarcoma recover under irradiation." Nevertheless, a review of the literature with this point in mind revealed not a single example of irradiation as the method of treatment in an early authentic example of osteogenic sarcoma.

The subject of this report, the history of which follows, came to treatment relatively early after the onset of the disease. When it presented itself it had the clinical radiological and histological characteristics of osteogenic sarcoma. The type of irradiation employed was first interstitial with radium element followed by application of "deep" X-ray.

CASE REPORT

S. W., Out-Patient Department, No. A72030, white girl, aged 11 years, presented herself to the Washington University Dispensary, February 2, 1922, complaining of swelling about the right knee. The family and previous history were of no moment. A month before entry patient fell and hurt the region of the right knee which gradually swelled and became painful on its inner aspect. Physical examination revealed only the condition about the right knee. There was a diffuse swelling of the upper medial aspect of the tibia. The knee joint was unaffected. There was slight tenderness to pressure. X-ray examination was made (Fig. 1). The Wassermann was negative. Pain became severe and patient entered the Jewish Hospital, February 21, 1922. At this hospital the tumor of the tibia was explored and found to have the characteristics of a malignant bone tumor. In spite of a prior consent, amputation was refused. Material for histological study was removed and it proved to be osteogenic sarcoma (Fig. 2).

The patient was referred to the St. Louis Children's Hospital for irradiation (Figs. 3, 4, 5, and 6). As the tumor had already been traumatized and manipulated by the exploratory operation it seemed that radium implantation could scarcely add to the hazard of mechanical dissemination of tumor cells. It was, therefore, decided to irradiate interstitially. Accordingly over a period of 3 days 1,166 milligram hours of irradiation with radium element in needles was evenly distributed, as well as could be judged, throughout the tumor mass. A week later deep X-ray therapy was applied over both the lateral and medial aspect of the leg to the limit of toleration (Figs. 7 and 8). The patient was irradiated with heavy dosage of X-rays on four occasions from March, 1922, to April, 1923. She has been systematically observed and radiographed from the first observation up to the present time. At no time has there been evidence of pulmonary metastasis (Figs. 9 and 10).

On March 7, 1923, patient was found to be developing a bow leg to such an extent that corrective measures were indicated (Figs. 11 and 12). This deformity appeared to be due to arrested growth of the tibia in the zone which was the site of the tumor. There was arrest of bone growth on the inner half of the tibia, both interstitial and from the epiphyseal cartilage. A brace was applied to correct the bowing of the leg.

Routine examination of this patient was made on March 14, 1929. At that time the examination revealed a small collection of faintly calcified material lying medial to the inner tuberosity of the tibia. This increased to the extent noted in the examination of August 19, 1931 (Fig. 13).

Figs. 11 and 12. Roentgenograms of April 24, 1923. Anteroposterior and lateral views of tibia revealing condition of bone slightly more than a year after onset of disease. The bowing of leg is indicated.

Fig. 13, left. Roentgenogram of August 19, 1931. Calcified material in soft tissue medial to tuberosity of tibia.

Fig. 14. Roentgenogram of July 23, 1932. Shows calcification stationary.

Since that time the calcification has remained unchanged (Fig. 14).

Through an entirely fortuitous set of circumstances this patient had what appears to be the unique experience of receiving irradiation treatment for an early osteogenic sarcoma. According to the views of many writers, at least two things were done in this case which are contra-indicated, namely, exploration of the tumor without amputation following, and intratumoral implantation of radium needles. Under the circumstances as noted the radium implantation appeared harmless.

Biopsy is justified in suspected osteogenic sarcoma, for the diagnosis of this disease is at best a difficult one to make and few physicians have enough experience with it to permit of its early diagnosis on clinical data or even clinical and radiological data combined. Biopsy alone is not necessarily an accurate determinant of the nature of bone tumors. Coley's views on the importance of the gross appearance of these tumors as a factor in diagnosis has not received the endorsement it deserves. If biopsy and exploration is to be done on a suspected osteogenic sarcoma a plan of treatment should be formulated first and be capable of being immediately instituted if desired.

Kolodny has pointed out the fact that intensive irradiation may be highly injurious to surrounding healthy structures. Desjardins has reported a case with marked atrophy of the structures about the shoulder girdle in a case of osteogenic sarcoma (?) of the humerus after intensive irradiation. There was also sclerosis of the humerus. In the subject of this report there is also marked sclerosis of the tibia. This change, however, seems to have regressed, the affected portions of the tibia assuming the nearly normal striated bone texture of Figure 14. At no time has there been evidence of injury to the knee joint.

CONCLUSIONS

Few conclusions can be drawn from this isolated case. It seems to show that intensive irradiation applied early in the course of osteogenic sarcoma may result in recovery for an extended period (10 years). Tumor exploration and biopsy can be done in this disease without necessarily disseminating it. The same statement applies to intratumoral radium implantation, though the writer most emphatically believes that this should not be done unless the circumstances are extraordinary, as in this case.

Though irradiation may do great damage to adjacent and overlying healthy tissue, in young persons they can revert to an approximately normal condition and remain so.

It is exceedingly difficult for a radiotherapist always to secure histological diagnosis, hence he is too often working in the dark and is ignorant of just what he is accomplishing. Prolonged observation of patients is next to impossible. Perhaps there are more favorable results in osteogenic sarcoma than is thought to be the case.

The writer wishes to express his appreciation of the kindness of Dr. Malvern B. Clopton for the privilege of observing and reporting this patient. This patient was originally

on Dr. Clopton's service at the St. Louis Children's Hospital.

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PHYSIOLOGICAL REST AND THE PRESERVATION OF LOCOMOTION[1]

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THE fundamental and guiding principles of the prevention of deformity and the preservation of function of the apparatus of locomotion should interest both the general practitioner and the specialist. The orthopedic surgeon is primarily concerned in the correction of deformities and the restoration of function of the apparatus of locomotion, and, as a teacher, he instructs his students in the underlying mechanical and physiological principles which will prevent deformity and disability. The orthopedist has little opportunity to apply practically these principles as compared with the other members of the medical profession. However, he is more cognizant of their meaning and importance since too frequently he sees the crippling conditions which result from a lack of understanding and improper application of them. These principles were not emphasized to the medical student 20 years ago. Today they receive some emphasis and their application prevents many surgical hazards and gives much gratification. The field for their use is large and they are effectively applied as a part of the therapy for any disease or condition which may possibly terminate with partial or complete loss of the functions of the extremities and the spine. Paralyses, burns, nutritional disorders, bone infections, joint infections, injuries (to nerves, tendons, ligaments, bones, joints, and muscles), the arthritides, congenital deformities and other less common problems may often require the intelligent use of the principles to be considered in this paper.

Collectively the principles may be termed as "physiological rest." The principles of rest have been studied and practiced since the time of John Hunter (1728–1793). Sir Arthur Keith states in *Menders of the Maimed* that "it was the custom of John Hunter to prescribe 'rest' as a routine measure in the treatment of disablements of the motor system of the human body. John Hilton (1807–1878) regarded rest as the most powerful aid which the surgeon could bring to the aid of disordered tissues and Hugh Owen Thomas (1834–1891) made rest his creed and ritual." Rest as a part of the therapy for disorders of the apparatus of locomotion is at present too often neglected because of insufficient knowledge of its meaning. In general the conception of the term "physiological rest" is incomplete and confused. The program of physiological rest will vary according to the particular disorder but the underlying principles expressed in the following general outline are constant. The principles are mechanical and physiological; the therapy is applied anatomy and physiology.

Physiological rest.

1. Surgery (manipulative or open) when indicated.
2. Fixation in the optimum positions—(a) optimum positions when restoration of function is anticipated; (b) optimum positions for ankylosis.
3. Maintenance of the integrity of the neuromuscular, vascular, and articular systems.

The writer believes that a therapeutic program as outlined will help the physician to understand more clearly the fundamental principles that are important in preserving the functions of locomotion; and it will make for order and clarity in the minds of the medical students as to treatment of diseases affecting locomotion.

Contractures and loss of function of the fingers and shoulder joint following treatment for Colle's fracture are evidence that part 3 of the program outlined was neglected. Extensive scar tissue webs binding the chin to the base of the neck or the arm to the side of the thorax could be avoided if part 2 were properly included in the therapeutic program of treatment for burns. The period of disability and hospitalization of patients with hæmatogenous osteomyelitis could be reduced if part 1 of the program were adequately executed. A large list of illustrations could be presented to demonstrate that the reason for numerous

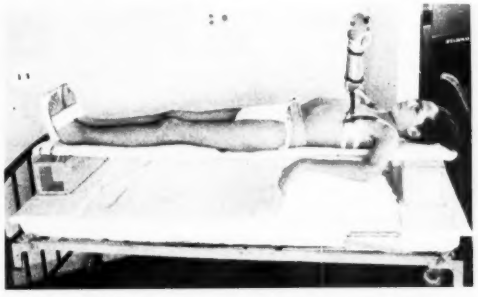

Fig. 1. Patient with extensive paralyses of both lower and right upper extremity during the acute tender paralytic phase of anterior poliomyelitis. The affected extremities are immobilized in the optimum positions for restoration of function. Proper fixation will prevent contracture deformities.

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Fig. 2. A, Residual paralyses of infantile paralysis with multiple preventable contracture deformities of spine, hips, knees, and feet. B, Patient after mechanical and surgical correction of the deformities. Patient had not walked since infancy. The contracture deformities were preventable.

surgical hazards and loss of function of one or more parts of the locomotor apparatus has been negligent application of one or more of the three phases of "physiological rest."

The principles of fixation vary according to whether restoration of function is or is not anticipated. Accordingly there are optimum positions for fixation when return of function is expected and optimum positions for ankylosis. The positions for fixation of fractures depend upon the type of fracture and the anatomical region fractured. It is not the purpose of this paper to review the numerous positions of fixation for all fractures but to emphasize the need of a clearer conception of the general treatment of fractures by means of physiological rest.

The optimum positions for fixation of the extremities and spine during the acute paralytic stage of infantile paralysis are shown in Table I. These positions are optimum because the lower extremities are in the most useful positions for the function of walking. The pelvis is on a transverse plane and the hips are abducted to favor the gluteal muscular mechanism which plays an important rôle in stabilizing the pelvis during the process of walking. The normal physiological curves of the spine are preserved. The shoulder is abducted and the elbow is flexed for the purpose of favoring those muscles which must function against gravity. The wrist and hand are immobilized in the physiological position of grasp with the thumb in the position of opposition and

TABLE I.—OPTIMUM POSITIONS FOR FIXATION WHEN RETURN OF FUNCTION IS ANTICIPATED (INFANTILE PARALYSIS, ACUTE TENDER STAGE)

Shoulder
1. Abduction 90 degrees.
2. External rotation 45 degrees.
3. Anterior flexion (elbow in front of anterior axillary line).

Elbow
1. Flexion 90 degrees.
2. Supination.

Wrist
1. Extension 30 degrees (dorsiflexion).
2. Neutral as to radial and ulnar deviation.

Physiological position of grasp

Hand
1. Fingers in semiflexion.
2. Thumb in position of opposition.

Spine
1. Straight with the normal curves not exaggerated.

Pelvis
1. Transverse plane.

Hip
1. Abduction.
2. Neutral as to rotation.
3. Neutral as to flexion and extension.

Knee
1. Straight with support under popliteal concavity.

Foot and Ankle
1. Dorsiflexion 90 degrees.
2. Neutral as to inversion and eversion. Arches well supported. Toes side by side and extended.

the fingers semiflexed (Fig. 1). Failure to apply these principles results in the development of contracture deformities which cause partial or complete loss of function of the upper and lower extremities and the trunk, as demonstrated in Figures 2a and b.

Figure 3 demonstrates the principles of splinting for Erb's brachial plexus birth paralysis where return of function is anticipated. Flaccid paralyses resulting from lesions of the peripheral nerves should be immobilized in the position of relaxation as demonstrated in Figures 4a—4b. Relaxation of a partially paralyzed muscle facilitates restoration of function while stretching favors further paralysis.

Burns involving the axillary region should be treated with the arm abducted and externally rotated in order to prevent fixation of the arm to the thorax by scar tissue as seen in Figure 5.

Bowing of the extremities and disturbances of the normal weight bearing lines can be prevented

TABLE II.—THE OPTIMUM POSITIONS FOR ANKYLOSIS OF JOINTS

Shoulder
- Abduction.
  - (a) Adult 45–50 degrees.
  - (b) Child 60–75 degrees.
- 2. External rotation—15 degrees.
- 3. Anterior flexion (arm in front of anterior axillary line).

Elbow
1. Occupation.
2. Right or left handed.
3. Flexion 90 degrees with hand in mid-pronation. Ankylosis of both elbows—one slightly more and the other slightly less than a right angle.

Wrist
1. Dorsiflexion 45 degrees.
2. Neutral as to ulnar and radial deviation.

Hand
1. Position of grasp altered by occupation.

Spine
1. Position in which normal curves are slight. Slight forward flexion of head and neck to accommodate walking and reading.

Hip
1. Adult.
   - (a) Flexion 45 degrees sitting occupation.
   - (b) Flexion 15–25 degrees standing occupation.
   - (c) Abduction 5–10 degrees.
   - (d) External rotation 5 degrees.
2. Child.
   - (a) Flexion 25 degrees.
   - (b) Abduction 5–10 degrees.
   - (c) External rotation 5 degrees.
3. Age.
   Occupation.
   Degree of shortening.

Knee
1. Occupation.
   - (a) Straight—standing occupation.
   - (b) Slightly flexed—sitting occupation.
2. Child—complete extension.

Foot and ankle
1. Plantar flexion 5–10 degrees (altered by sex and shortening of extremity).
2. Neutral as to inversion and eversion. Arches supported. Toes extended and side by side.

during the active phase of rickets if the infant is immobilized on a Bradford frame or in a plaster-of-paris spica and not permitted to be weight bearing on the softened bones.

Deformity and loss of function of an anatomical part are frequently inevitable. Destruction and loss of function of the affected joint is the usual end-result in joint tuberculosis. Gonorrhœal arthritis, ankylosing atrophic arthritis, compound intra-articular fractures, and non-specific joint infections not infrequently result in fibrous or bony ankylosis. Ankylosis of a joint may greatly

Fig. 3. Brachial plexus birth paralysis is best treated with the affected extremity immobilized in the optimum position for restoration of function as illustrated.

or only slightly interfere with the functions of the apparatus of locomotion. The degree of disability depends upon the position of ankylosis of the affected joint. Loss of function of the hand is minimum and slight if the wrist is ankylosed in the position of dorsiflexion; but ankylosis of the wrist in extreme plantar flexion results in very marked loss of function of the hand. Ankylosis of the hip joint in one position may force the patient to walk with the aid of crutches, while ankylosis in another position may be associated with only moderate disability. The positions of ankylosis which cause the minimum of interference with the functions of the apparatus of locomotion are known as the optimum positions for ankylosis and may be outlined as in Table II.

Figure 6 represents the proper application of the principles of fixation when ankylosis of the hip is anticipated in a child with infectious arthritis of the hip joint.

The optimum position for ankylosis of certain joints varies according to age, sex, and occupation. The knee, during childhood, should not be ankylosed in flexion since with continued weight bearing the flexion deformity increases at the level of the epiphyseal discs. The position for ankylosis of the ankle varies in men and women because of the difference in the height of the heels of the shoes. The adult patient should always be

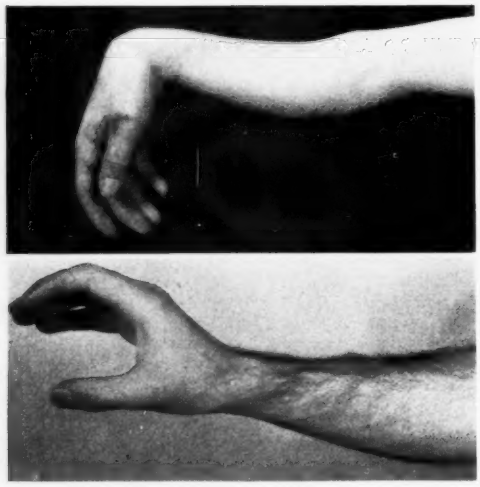

Fig. 4. A, Radial nerve neuritis with wrist drop. B, Should be treated with the wrist splinted in the optimum position for relaxation of the paralyzed muscles.

consulted regarding his occupation before the position for ankylosis is definitely determined.

The principles included in part 3 of the program of physiological rest are generally grouped under

Fig. 5. Note the preventable scar tissue web between arm and thorax complicating an extensive burn. Axillary burns should be treated with the arm in the optimum position for return of shoulder joint function (abduction and external rotation).

Fig. 6. The right hip joint immobilized in the optimum position when ankylosis is anticipated. Proper fixation will prevent ankylosis in poor functional position.

the heading of physical therapy. They include numerous measures which favorably influence the physiology of the various tissues which control the functions of the apparatus of locomotion. Assiduous attention to these measures often determines the success or failure of treatment. The integrity of the circulatory, neuromuscular, and articular systems can be maintained in the presence of certain disorders if mechanical and physiological principles are intelligently applied. These measures may be conveniently outlined as follows:

PHYSICAL THERAPY

I. The normal stimulus of function
   A. Weight bearing
      1. Partial
      2. Full
   B. Active muscular contractions
      1. With joint movements
      2. Without joint movements
      3. Assisted
      4. Unassisted
II. Elevation
III. Massage
IV. Heat—induced fever
   A. Local
   B. General—systemic
V. Cold
VI. Alternating heat and cold (contrast baths)
VII. Electrotherapy
VIII. Heliotherapy
IX. Occupational therapy
X. Under water gymnasium or therapeutic pool

Stiff and useless fingers should never result after proper treatment of a Colle's fracture if the patient is instructed actively and completely to extend and flex the fingers several times daily while the fractured part is splinted. The same patient will not lose the functions of abduction and external rotation of the shoulder on the affected side if the patient is instructed actively and frequently to place the hand to the mouth and back of the head while the Colle's fracture is immobilized. These principles are expressed in a phrase which may be applied to most fractures—"actively mobilize the muscles while the fractured bone is immobilized."

Muscles of an extremity can be actively contracted although the extremity is firmly immobilized in apparatus. This is often highly desirable in order to maintain muscle tone, to prevent atrophy and muscular contractures, and to maintain the integrity of the neuromuscular and articular systems. Several days after surgical treatment for internal derangements of the knee joint, the patient is instructed actively to contract the quadriceps muscle. Subsequent knee joint function depends upon the integrity of the extensor apparatus of the knee joint. Many patients who had torn semilunar cartilages treated surgically experienced continued disability because the quadriceps mechanism, paralyzed by the local surgical shock, was not re-educated.

The principle of elevation is simple and obvious but the lack of its application is seen daily.

Restoration of function following a supracondylar fracture of the elbow as well as many other fractures is aided by active motions under warm water. The heat stimulates the circulation and the buoyancy of the water relieves much of the weight of the extremity and gravity; as a result active motion is accomplished with less muscular effort and with less pain.

A child with residual paralyses of anterior poliomyelitis may be able actively to contract, exercise, and develop partially paralyzed muscles under water but out of water the same muscles could not function against gravity and the weight of an extremity. Septic joints, hand infections, osteomyelitis, paralyses, fractures, and other conditions affecting locomotion will often show remarkable improvement if treated under water at the proper time during the therapeutic program. The number of illustrations to show the practical applications of these various principles is unlimited while the vast number of principles involved in surgical judgment and surgical technique will not even be considered.

The purpose of this paper is not to consider the details of management of any stage of treatment of the many disorders of locomotion but to present a general outline of the program of therapy which will tend to diminish the number of preventable surgical hazards.

The three phases of the program of physiological rest and the numerous principles implied in each should guide the clinical course of all patients suffering with disorders of the apparatus of locomotion.

OVARIAN TERATOMATOUS CYSTS OCCURRING IN CHILDREN

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IT HAS been estimated that of all tumors affecting the ovary, 7 per cent consist of dermoid and teratomatous cysts. Such tumors are rarely met with before puberty, although they may occur at any age. McKee, when describing a case in a child aged 7 years which came under his care in 1899, stated that 52 cases only, had been previously recorded. Since that time, however, further cases have been recorded but the total number at the present time is still under 100.

At the Hospital for Sick Children, Great Ormond Street, not a single case has been met with in the last 25 years, either on the clinical side or discovered at autopsy. At King's College Hospital 1 case only (Case 2) has been seen in 25 years and no other case is to be found in the postmortem records. At the Belgrave Hospital for Children, 1 case only (Case 1) has been seen in the last 25 years and no cases have been recorded in the postmortem files.

From the records of these three hospitals, dermoid and teratomatous cysts of the ovary are apparently very rare in young subjects. On account of their relative rarity I have deemed the following cases worthy of publication. Two cases have come under my own personal supervision, while the third case, which was under the care of Miss M. Glen Bott, of Nottingham, to whom I am greatly indebted for kindly allowing me the opportunity of publishing it, was of especial interest as it was similar in many respects to one of my own.

Teratomatous cysts are frequently called "dermoids," but such a designation is a misnomer and should be discarded. A dermoid is strictly speaking, an inclusion cyst, the walls of which contain structures derived from the ectoderm only. The existence of such a cyst in the ovary has yet to be proved.

Teratomatous cysts contain elements derived from the ectoderm, in the form of skin or of its appendages; from the mesoderm, represented by unstriped muscle, cartilage and bone; and from the entoderm, exemplified by intestinal and respiratory mucous membrane.

The term "embryoma" is frequently used to designate these tumors, and is perhaps a more significant term than "teratoma." Both these terms, however, are applied to a group of neoplasms composed of heterogeneous tissue elements.

A teratomatous cyst is always composed of two definite parts: (1) an intracystic rudiment in which representatives of all three primitive layers of the blastoderm can be demonstrated; (2) a cyst wall which encloses the embryonal rudiment.

These cysts are occasionally bilateral but are more usually unilateral. The mode of origin of such cysts has given rise to much speculation in the past, but up to the present time no theory concerning their causation is quite convincing. Probably the theory conceived by the late Professor Shattock is the most satisfactory. He suggested that an embryoma may be due to the fertilization of one of the primordial ova in the ovary of the developing embryo; the result being that the embryo gives rise to a second imperfect individual whose origin is not synchronous with itself but is of a later date.

The 3 following cases all occurred in young girls. The cysts were removed by operation, and a careful histological examination was made in each case.

Case 1. Elizabeth M., aged 9 years, was admitted to the Belgrave Hospital for Children in May 1925 on account of a hard abdominal tumor which been been noticed for some 4 months previously. She was the eldest child of a family of four, all girls. Her mother was 32 when she was born, and had been operated upon at the age of 25 for a right ovarian cyst. The child's mother, when first she brought her daughter to the hospital, volunteered the remark that she thought her girl had the same trouble as she had had herself, and therefore requested that an operation should be performed for its removal. This is the first case of a teratoma of the ovary occurring in both mother and child, which has been put on record.

When first seen at the hospital the girl was found to be an intelligent, well built and athletic child. She stated that she first noticed a lump in her abdomen shortly after Christmas, 1924, when lying in a bath. Previously to that date, she had no idea that there was a lump in her body, and it had caused her no trouble or inconvenience whatever.

On examination, a large hard tumor could be both seen and felt when the patient was lying down. The apparent size of the tumor was comparable to that of a large grapefruit. It was quite smooth and hard and was freely movable in the abdominal cavity. On pressing the tumor in an upward direction the patient complained of some slight discomfort. Rectal examination was negative. The growth of pubic hair was extensive; the breasts were well developed and appeared to be about the size of those of a girl at

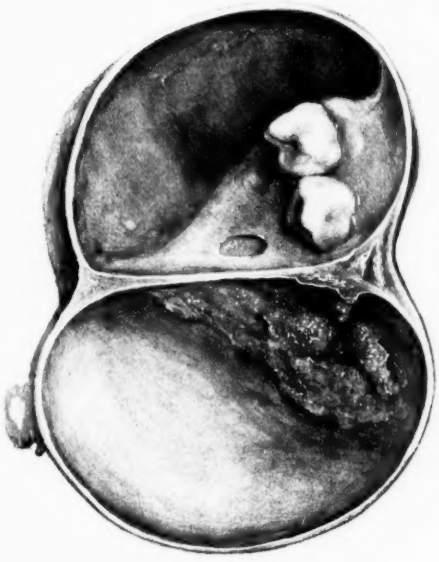

Fig. 1. Drawing of teratomatous cyst of ovary. A section has been made through the center of the tumor (Case 1). The two main cysts are divided by a thick septum. Two large molar teeth can be seen in the upper cyst.

puberty. Menstruation had not commenced. There were no symptoms referable to the alimentary tract. The bowels were open daily without the aid of purgatives. As the girl was in her school net-ball team she must have taken a considerable amount of strenuous exercise every week. The kidneys could not be palpated and the urine was normal. There were no symptoms of any pressure on the bladder.

On May 25 the abdomen was opened by a paramedian incision and a large right ovarian tumor was exposed. The tumor had a thick pedicle which was so long that it was quite an easy matter to deliver the tumor outside the abdominal cavity. The pedicle was clamped between two pressure forceps and the tumor removed. The pedicle was transfixed and the cut end was so carefully sewn over that no raw surface was left exposed. The uterus and other appendages appeared quite normal. The whole abdominal cavity was explored but no other abnormality could be discovered. The wound was closed in layers with interrupted sutures. The patient made a rapid recovery, and was able to leave hospital 16 days after the operation.

She was brought up to hospital again in July, 1925, as she had had a period which lasted 4 days, but otherwise appeared normal in every respect. She remained under observation for some long time. She kept quite fit and well and although she was not yet 10 years of age, her periods occurred regularly. Whether the removal of the ovarian teratoma had an influence on the early menstrual history of this patient or not, is a moot question.

The tumor measured 4 inches across, and weighed just over a pound. It was hardened in formol solution and some 10 days later was subdivided by a median section.

Fig. 2. Microscopical drawing (×25), of the wall of the cyst in Case 1. The edge of the cyst is partially covered with thick stratified epithelium showing keratinization. The section exhibits two gland ducts, lined by high columnar epithelium and areas of dense leucocyte infiltration.

It was found to consist of two cysts, an upper and a lower (Fig. 1). The walls of the cysts were very thick and fibrous. Inside the upper cyst was a solid elevation on the summit of which two well marked molar teeth could be seen. The lower cyst contained thick mucoid fluid and on the inside, at one place, there was an irregular thickening which on section was found to be cartilaginous. No hair was found in any part of the tumor.

Microscopically the tumor exhibited the characteristics of a teratoma. The lining of the cyst was in places columnar ciliated epithelium; in others it was composed of stratified epithelium (Fig. 2). Sebaceous glands and also some nervous tissue could be seen. In other sections distinct areas of cartilage were found but in no part was there any evidence of bone. In all probability, bone would have been found in the region of the molar teeth, but as the specimen was preserved intact, as far as possible, micro-

Fig. 3. Drawing showing one-half of ovarian teratoma removed in Case 2. Multiple cysts can be seen.

scopical sections were confined to the region of the cyst wall only.

CASE 2. Elsie B., aged 8 years, was quite healthy up to the age of 5 years, when she commenced to suffer from constipation and required purgatives three times a week at least. She was treated for constipation at several hospitals and dispensaries but her condition did not improve.

Apart from the constipation, she enjoyed good health, and was quite a bright and intelligent child. On November 20, 1931, she was seized with abdominal pain and vomited several times. The vomiting was followed by some loose motions. The pain lasted a few hours only. Shortly afterward she was playing with other children and appeared to be quite normal. The mother gave her a bath in the evening and then noticed a swelling in her abdomen, which she was quite certain had not been there before. The child was sent up to King's College Hospital where she was found to have a large, hard abdominal tumor, about the size of a small cocoanut. It was movable from side to side, and slightly from above downward, but could not be displaced upward farther than the brim of the pelvis. The tumor appeared to be cystic in places. Since the appearance of the tumor the child's bowels had acted normally every day without the aid of any purgatives. Rectal examination was negative.

The girl was shown at a meeting of the Children's Section of the Royal Society of Medicine, on the 27th of November, 1931, as a case of dermoid cyst of the ovary. The consensus of opinion, however, was that the tumor was a mesenteric cyst.

The history of this case is all important since I came to the conclusion that the cyst had been within the pelvic cavity for several years, and was there the cause of the habitual constipation. When it suddenly rose out of the pelvis, as it undoubtedly did, it brought about a certain amount of shock which caused the child to vomit. If the tumor had slowly developed within the abdominal cavity proper, the child's mother who bathed her every night, would certainly have noticed a swelling before. The subsequent relief of the constipation due to the diminution of pressure within the pelvic cavity is especially worthy of note.

On December 2, 1931, a laparotomy was performed under open ether anæsthesia. The abdomen was opened through a right paramedian incision, and a large right ovarian cyst, weighing just over 2 pounds, was removed. The left ovary was normal. No other abnormalities within

Fig. 4. Microscopical drawings of different parts of the wall of the tumor in Case 2 *A*, above, microscopical drawing showing dilated capillaries in a dense fibrous tissue stroma. *B*, microscopical drawing showing thin layer of stratified epithelium opening on to the surface of which is a sebaceous gland. Four hair follicles lying more deeply in the section can be seen. (×75).

the abdominal cavity could be found. The wound healed normally, and the child was able to leave hospital 14 days after the operation.

When the tumor was cut through its center was found to be mainly cystic with a hard solid formation at one part (Fig. 3). Microscopical examination of the wall of the cyst demonstrated its teratomatous nature. A number of cysts of varying sizes could be seen. One of the larger cysts was lined partly by columnar ciliated epithelium, and partly by a thick layer of stratified epithelium which, however, did not show much tendency to the production of keratin. Sebaceous glands in association with this stratified epithelium were present (Fig. 4). Some of the cysts had lost their epithelial lining, but some, especially the smaller ones, were lined by columnar or cubical epithelium. Some of the cysts contained a homogeneous pink-staining material resembling thyroid colloid, otherwise no definitely recognizable thyroid tissue was present. There was ample evidence

of nervous tissue and several areas of calcification were found. The solid portion within the cystic cavity was found to contain hair, cartilage, and bone.

A very similar case to the foregoing was recorded by Meigs in 1899, in a girl aged 10 years. An abdominal swelling was noticed by the child's mother, when she was undressing her. When the girl was examined at the hospital the swelling was thought to be a distended bladder. Catheterization was performed but a few ounces only of urine were withdrawn. Operation was performed, and a twisted ovarian teratoma, which contained sebaceous material, cartilage, and bone was removed.

A correct diagnosis of these cases seems to be one of supreme difficulty, and almost every variety of abdominal tumor has, at one time or another, been suspected without the real condition having been recognized.

CASE 3. Agnes W., aged 9 years, was admitted to the Children's Hospital, Nottingham, on the 31st of October, 1931, under the care of Miss M. Glen Bott, complaining of attacks of abdominal pain. The symptoms commenced insidiously in March, 1931. She complained of pain which had no relation to food but was accentuated by walking. The seat of the pain was situated just above the pubis, it was not relieved at night time, and she suffered from frequency of micturition. The bowels acted normally, and there was no history of vomiting.

On admission to hospital, the patient was found to be a well developed and healthy looking girl. A pear-shaped swelling could easily be palpated in the abdomen. It was movable from side to side, and slightly upward and downward. It was dull on percussion, but not tender. Rectal examination was negative.

An operation was performed through a subumbilical paramedian incision. A large right ovarian cyst was removed, measuring 4½ by 5 inches. The left ovary was slightly larger than normal. The abdomen was closed in layers, and the patient made an uninterrupted recovery and was discharged from hospital on November 11, 1931.

The cyst was unilocular with a smooth wall. Situated near the base of the cyst was a definite, hard, intracystic elevation covered with stratified epithelium. Beneath the stratified epithelium, a single tooth was found to be embedded in a matrix of bone and cartilage. There was a considerable amount of hair and sebaceous material which provided an embedding medium in which all the tissues were glued together in a mass.

McKee recorded a case in 1900 in a girl, aged 7 years, where an abdominal tumor was thought to be a sarcoma of the kidney. Operation proved it to be a cystic swelling of the ovary, containing skin, sebaceous material, cartilage, and bone. In some of the early cases which are recorded, tapping of these swellings was carried out; in some cases, because operative interference was not permitted by the parents of the child. Alcock in 1871, and Black in 1892, record cases where tapping was performed followed at a later date by removal of the tumor.

Owing to the systematic medical examination to which school children are now subjected it is very unlikely that ovarian cysts in young subjects will, in the future, be allowed to assume any large size.

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LATERAL ABERRANT THYROID GLANDS

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TUMORS of the neck arising from lateral aberrant thyroid glands are rare and I have been able to find but 49 cases in the literature. The group as a whole has long been recognized. Albert von Haller, in 1779, first observed anomalously placed islands of thyroid tissue in the neck. In 1839, Albers referred to misplaced thyroid tissue as accessory thyroid glands. Gruber, in 1845, reported 2 cases and in 1849, a monograph, accurately describing accessory thyroids, was published from Milan. In 1850, Stanley, of England, made the first extirpation of an aberrant thyroid gland. Occasional reports of clinical cases appeared up to 1897 when de Boncourt collected 15 cases of accessory lingual thyroids. A few years later, Storrs, Murphy, and Schrager made extensive clinical studies.

The importance of lateral aberrant thyroid glands demands the interest of the embryologist and pathologist as well as the clinician. Embryologically their origin and development is much discussed but far from settled. Pathologically they are greatly influenced by the activities of the thyroid gland. They also show a distinct tendency to malignancy. Clinically, their diagnosis is difficult and their prognosis favorable.

ORIGIN

Several theories have been advanced to explain the formation of lateral aberrant glands, these changing from time to time as additional information has been brought to light on thyroid embryology. It was once thought (His, Born, Prenant and others, that the thyroid originated from two sources, namely, a median portion from the floor of the pharynx and two lateral portions from the lateral outpouchings of the pharynx. At that time it was possible to explain the presence of lateral thyroid tissue by assuming fusion of the lateral and median portions of the gland had failed to take place and as a result lateral rests remained in the neck.

Later, following the discovery of the origin of the parathyroid glands from the third and fourth branchial clefts it was thought that the thyroid originated entirely from a single median anlage caudal to the anterior portion of the rudimentary tongue and that fusion played no rôle in its development. This theory necessarily discounted the belief that lateral rests were due to unfused thyroid tissue. More recently the so called fifth pouch, or ultimobranchial body, has been claimed to play a part in thyroid development but upon this subject embryologists give decidedly conflicting opinions.

With the embryology of the thyroid still unsettled, the origin of lateral aberrant thyroid glands likewise remains disputed. At present evidence points strongly toward the origin of the lateral aberrant thyroid from the fifth pouch or ultimobranchial body. This theory is supported by Leech and his co-workers as follows: "The thyroid in its development is constantly associated with the migration and fusion of epithelial cells derived from the so called fifth pouch or posterior outpocketing of the pharyngeal complex (the ultimobranchial body); these epithelial masses may vary considerably in number and position; the lateral aberrant thyroid glands tend in a high percentage of cases to undergo papilliferous and cystic degenerative change, a lesion never associated with lingual thyroid tissue. These facts, it would seem, serve to identify these tumors as a specific group and to account for their origin on sound embryonic evidence."

SYMPTOMS AND DIAGNOSIS

Many lateral aberrant thyroids produce no symptoms. As they increase in size they may cause the patient to consult a physician on account of swelling in the neck. Few produce sufficient pressure on the trachea and vessels of the neck to cause symptoms. Their growth is slow, over a period ranging from several months to several years without signs of thyroid disease. They are usually situated in the anterior triangle of the neck and may occur as single tumors or as a chain of nodules. On palpation they are not tender and may be firm or soft in consistency. There are no constant clinical characteristics to differentiate lateral aberrant thyroid glands from tuberculosis, lymphadenoma, metastatic carcinoma, Hodgkin's disease, or other conditions which may give rise to tumors of the neck; consequently diagnosis is extremely difficult and rarely made. As an aid in differentiating these tumors of the lateral aberrant thyroid glands from other enlargements of the neck, Schrager has emphasized the following: "(1) The tumor is likely to increase in size at puberty. (2) It tends to fluctuate in size

during menstruation. (3) It tends to become cystic. (4) It is usually unilateral; if solid not greater than the size of a mandarin orange. (5) It is of slow growth, smooth, and, if not cystic, of soft consistency."

PATHOLOGY

Briefly, lateral aberrant thyroid glands may be single or consist of a chain of glands connected by strands of thyroid tissue. In size they may vary from a few to 10 or more centimeters in diameter. They are encapsulated in a very vascular, reddish green capsule and are firm or soft depending upon the amount of cyst formation which has taken place. Often they resemble normal thyroid tissue. Microscopic sections show a marked papillary growth of columnar epithelial cells in a vascular connective tissue stroma with evidence of slow growth as manifest by calcification, hæmorrhage, hyalinization of stroma and cystic degeneration. The tendency of these tumors to undergo malignant degeneration is great, and it is not uncommon to find mitotic figures and other signs of malignancy in what may otherwise appear to be a benign tumor.

During the past 10 years, 3 cases of tumors of aberrant thyroids have been observed in the Presbyterian Hospital. These patients have been followed for 10, 9, and 7 years, respectively. One of the patients subsequently developed marked hyperthyroidism from which she made a good recovery after subtotal thyroidectomy. Another writes that she is in excellent health and has had no illness since her operation. The third cannot be located at the present time. He was in good health for 7 years after his operation.

REPORT OF CASES

Case 1. I. J., a woman aged 30 years, entered Presbyterian Hospital complaining of a tumor of the left side of the neck which had been present for several years gradually increasing in size during this time but with a more rapid increase during the past 6 months. She had no other subjective symptoms, the tumor had caused her no pain, and she stated that her general health had always been good. During childhood she had had measles and chickenpox and at age 17 years, an appendectomy. Her father, mother, two sisters, and a brother were living and well and no history of tuberculosis, malignancy, or thyroid disease in the family was known.

The patient was a well developed, well nourished woman with a tumor mass behind the angle of the left jaw about the size of a hen's egg. On palpation the tumor mass was found to be medial to the upper portion of the sternomastoid muscle. It was firm, freely movable, showed no redness, and was not tender. The thyroid gland was palpated in its normal position. The teeth were good; the tonsils showed no infection; the heart borders were normal. There was an appendectomy scar in the right lower quadrant of the abdomen. Reflexes normal.

The urine was normal, the hæmoglobin, red, white and differential blood counts were normal. X-ray picture of the chest showed a small, old, healed tuberculous process of the left apex.

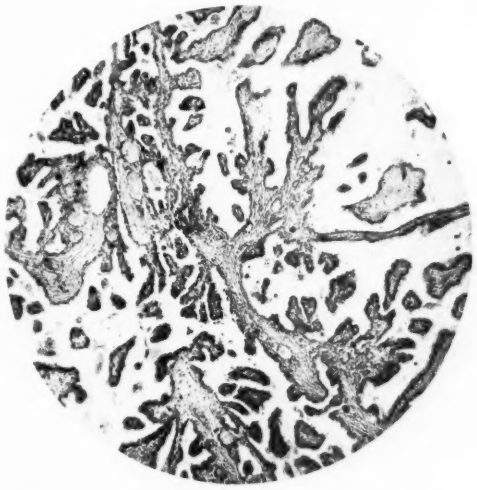

Fig. 1. I. J. Showing extensive growth of cuboidal epithelial cells arranged in papillæ and alveoli.

Under local anæsthesia, an incision was made in a vertical direction through the skin and fascia. The tumor mass was exposed and carefully dissected out.

The specimen consisted of a mass measuring 4 by 3 by 2 centimeters. It was red and rather firm. The surfaces made by sectioning were moist, reddish brown, and in portions resembled normal thyroid tissue while in other areas the tissue was soft and friable and contained small cysts. Microscopic sections showed extensive growth of cuboidal epithelial cells arranged in papillæ and alveoli. The connective tissue was slight in amount. There were several fairly typical acini seen (Fig. 1).

Case 2. G. P. E., a man, aged 32, entered Presbyterian Hospital complaining of a swelling in the left side of the neck of 7 years' duration, which had been gradually increasing in size during these years but had caused him no pain or discomfort in any way. During the past 2 months he noticed the increase in size of the tumor more than previously. During childhood he had had measles and mumps and an occasional sore throat. His father and mother were living and well. There was no history of tuberculosis, carcinoma, or thyroid disease in the family.

The patient was well developed and well nourished. A firm, movable tumor about the size of a plum was found on the left side of the neck posterior to the angle of the jaw. Below this was a second tumor of the same description about the size of a hazel nut and along the anterior border of the sternomastoid muscle about 2.5 centimeters above the clavicle was a third tumor the size of a small plum and of similar consistency. The thyroid gland was palpated in the normal position. The tonsils were absent; teeth good; heart borders normal. A slight systolic murmur was heard over the apex. Pulse was regular, rate 72. Blood pressure was 102 systolic, 70 diastolic. The lungs were normal. No tenderness or masses were noted in the abdomen. The reflexes were normal.

The urine was normal; the hæmoglobin, red, white, and differential blood counts were normal. Blood Wassermann

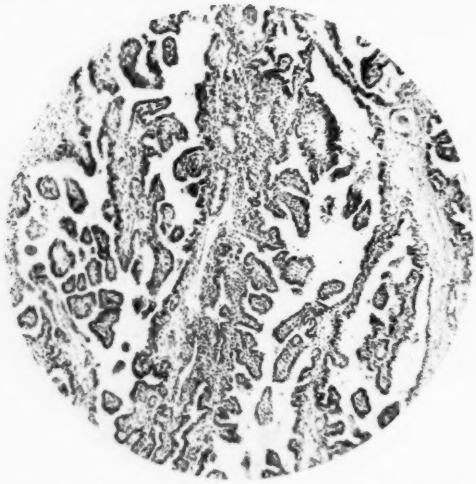

Fig. 2. G. P. E. Showing papillary growth of cuboidal epithelial cells which in certain areas suggest malignancy.

Fig. 3. M. B. Showing marked growth of cuboidal epithelial cells in papillary and cystic formation.

was negative. X-ray examination of the chest showed a slight increase in hilum shadows but otherwise was negative.

Under ether anæsthesia, an incision was made along the anterior border of the left sternomastoid muscle and seven glands were removed from beneath the muscle in its course through the neck.

The specimen consisted of seven nodes of various sizes, the largest being 5 centimeters in diameter. They were red and firm. Surfaces made by sectioning were moist, reddish brown, and contained a few small cysts in which there was a brown fluid. Microscopic sections showed marked papillary growth of cuboidal epithelial cells growing on a markedly vascular connective tissue stroma. In the base of some papillæ were found groups of apparently normal acini lined with cuboidal epithelial cells and filled with colloid. The papillary structure in certain areas suggested malignancy (Fig. 2).

Case 3. M. B., a woman, aged 36 years, entered Presbyterian Hospital complaining of a swelling in the left side of the neck present for 15 years or possibly longer. This swelling was first noticed during puberty and seemed to be slightly larger during her menstrual periods. Aside from this slight fluctuation the mass had not changed in size to any noticeable extent. She had reduced 25 pounds by dieting 2 years previous to her admission to the hospital. Since that time the swelling had been noticed by her friends and she had been quite conscious of it. She thought at times she had a slight choking sensation due to pressure of the tumor. Her general health had always been good. She had had chickenpox during childhood and an attack of influenza 6 years previously. A dilatation and curettage had been done following a miscarriage. There was no history of other pregnancies. Patient's husband had died of malaria. Her father, mother, one brother, and two sisters were living and well and there was no history of tuberculosis, carcinoma or thyroid disease in the family.

The patient was a well developed, well nourished woman with a tumor mass about 2.5 centimeters in diameter on the left side of the neck anterior to the middle third of the sternomastoid muscle and a second tumor slightly smaller at the angle of the jaw. On palpation these tumors were slightly soft, freely movable, and not tender. Apparently there was no pressure being exerted by these on the trachea. The thyroid gland was palpated in the normal position.

The tonsils were not infected. The heart borders were normal; no murmurs were heard. Blood pressure was 120 systolic, 85 diastolic. The pulse was regular, rate 84. The lungs were normal. No masses or tenderness were noted in the abdomen. The reflexes were normal.

The urine was normal; the hæmoglobin, and the red, white, and differential blood counts were normal. Blood Wassermann was negative.

Under local anæsthesia, an incision was made along the left sternomastoid muscle and the two tumor masses were removed by careful dissection.

The specimen consisted of two masses, each measuring approximately 4 centimeters in widest diameter. The tissue was red brown and firm for the most part, having a few small soft areas. The surfaces made by sectioning were moist and red brown. In the soft areas considerable brown fluid and small cysts exuded. Microscopic sections showed marked cuboidal epithelial growth in papillary and cystic formation. The connective tissue was considerably increased and vascular (Fig. 3).

TREATMENT

In any case of suspected aberrant thyroid the presence of a thyroid gland in its normal position should be determined. Once this has been established all doubtful masses in the neck should be removed. It is well to remember that pathology in the thyroid gland proper may cause enlargement with changes of the associated aberrant gland and in these cases it is well to proceed with considerable care. The location of these glands makes injury to the spinal accessory nerve and jugular vein easy. Another common complica-

tion is profuse bleeding. Because of the cystic structure of these glands aspiration has been attempted but this should not be done for it is both useless and not without danger. Following surgical removal all patients should be subjected to a series of X-ray treatments such as are given for malignancy even though the tumor appears to be benign. These postoperative X-ray treatments are of great importance as these tumors are radiosensitive.

SUMMARY

The tendency of lateral aberrant thyroid glands to undergo malignant degeneration has already been called to attention repeatedly but so important is this fact that it cannot be overemphasized. Although to all appearance these glands may be benign they have been known to recur after removal and produce metastases. That generally accepted benign tumors of the thyroid, such as enchondromata and myxomata, may become malignant is well known and years ago Cohnheim called attention to metastases arising from adenoma gelatinosum of the thyroid, a benign tumor. Hinterstoisser in an extensive study of carcinoma of aberrant thyroid tissue observed that carcinoma of aberrant glands is less malignant than carcinoma of the thyroid gland proper. Recently, Leech and others, after a careful study of malignant tumors of the thyroid, have pointed out the similarity between papilliferous adenomata of the thyroid and tumors of lateral aberrant thyroid tissue suggesting the possibility of a single origin for both groups of tumors from pharyngeal epithelial rests of the fifth pouch.

CONCLUSIONS

1. Lateral aberrant thyroid glands are extremely rare. They are of great clinical as well as of embryological and pathological importance. They are difficult to diagnose and tend to become malignant but with good surgical therapy they offer a relatively good prognosis.

2. In the presence of a thyroid gland in its normal position, suspected masses in the neck should be removed. X-ray treatment should be given following removal in all cases.

3. Three additional cases of lateral aberrant thyroid glands are presented.

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RICHTER'S HERNIA

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RICHTER'S hernia is a rare, unusual type of hernia. In spite of its rarity, an understanding of its pathology and the symptoms associated with it is important since any delay in recognition may result in very serious consequences. While Richter's hernia is a form of strangulated hernia, it is characteristically associated with partial intestinal obstruction rather than with complete obstruction which is usually present in strangulated hernia. Richter's hernia may be described as a hernia in which only a part of the circumference of the bowel is engaged and strangulated, and this involved portion may rapidly become gangrenous although the lumen of the gut remains open to some degree. The portion of the engaged bowel resembles a small diverticulum of the wall (Fig. 1). Only those hernias that meet the description given should be included under this name.

In the early literature there was much confusion concerning this type of hernia, since many types were reported under this name; for instance, cases of small hernia, partial enterocele, incomplete hernia, pinching hernia, Littre's hernia, and the like, have been reported as Richter's hernia. After an exhaustive review of the early literature, Treves found 80 cases, in 53 of which the reports were complete enough for satisfactory identification and study. He included 4 operative cases of his own and gave a clear clinical picture of this condition. Three of his patients died after operation, while the fourth, in whom previous to operation a reduction of the hernia had been done *en masse*, recovered following operation.

In 1700 Littre described 3 cases in which only a portion of the bowel wall was found in the hernia sac; 2 of these were hernias later recognized as involving Meckel's diverticulum but the third could not be identified from his report. He believed that these diverticula were the result of the intestinal wall being pulled out into a sac. It was not until 1815 that Meckel described the diverticulum that now bears his name, thus explaining the true nature of Littre's 2 cases. The first complete scientific description of this type of hernia was made by Richter in 1778. He described this form of hernia as a "small rupture."[1] In his book on hernia, one chapter concerned the diagnosis and treatment. He recognized that the wall of the involved gut was made up of the same layers and structure as were present in the intestinal wall a condition not present in the diverticulum later described by Meckel. In considering treatment, he recommended, if gangrene had not appeared, reduction aided by dilatation of the ring with a hook, but if gangrene was present he believed that reduction was dangerous and that resection should then be done. Treves suggested that this type of hernia be called Richter's hernia in order definitely to identify it and to differentiate it from the hernia of Littre and other forms. The earliest report Treves was able to find was that of Guilielmus Fabricius Hildanus in 1606.[2] In the fifty-fifth observation of his first one hundred surgical cures, he described the case of an elderly woman who had a strangulated hernia which discharged into the groin, after which the patient had complete relief of symptoms. The intestinal fistula thus formed remained open for only 2 months following the scarification of the swelling; it then healed and the patient made a complete recovery. While the exact relation of the bowel to the hernia was not observed, the fact that the fistula closed indicated that only a portion of the bowel wall was in the hernia.

In 1899, R. S. Fowler reported under the title "Partial Enterocele" 2 cases with this condition. He again made an exhaustive review of the literature and included a full bibliography in chronological order, including 94 references. He presented an excellent clinical picture of the condition, which was similar to that presented by Treves. R. H. Fowler, in 1913, described 2 cases; one involving the cæcum and the other the appendix. A review of the literature after 1899 was made by Rhodes in 1928. He was able to find 45 additional references since Fowler's report in 1899, and reported the histories of 3 patients with true Richter's hernias and 3 patients with a knuckle of small intestine in ventral hernias. The confusion which was present in the early literature was again evident in Rhodes' report since many of the reports that he included were of Littre's hernia. Bissell reported 2 additional cases in 1929, while Orr added 1 in 1930. After a review of the old and new literature on this subject, it will be seen that little attention has been

[1] This book was obtained from the Library of the New York Academy of Medicine.

[2] This book was obtained from the Boston Medical Library

p d to it since 1899; few reports were found, only 1 operations for this condition being reported. T s by no means represents the actual incidence o number of patients seen and treated. So little a ention has been given the subject that un- d btedly many patients are treated for simple st ngulated hernia. Many of the standard text- b ks in surgery do not mention the subject but w believe it is sufficiently important to report th cases seen.

Case 1. An American laborer, 60 years of age, was exam ed in March, 1927. He had been well until 24 hours pre ious to this examination when he developed a pain in the left lower quadrant. On the day that he was seen he had vomited several times. He had not been aware that he had a hernia. On physical examination he appeared to be acutely ill. His tongue was clean and there was no fæcal odor to his breath. The abdomen was soft throughout; there was no visible peristalsis and no distention. A small swelling about 2 centimeters in diameter in the left groin could not be reduced. There was localized tenderness over the swelling. Operation was performed (Dr. H. M. Clute) 24 hours after onset, incision being made directly over the femoral ring. When the sac was opened, a segment of bowel was seen engaged in the ring (Fig. 2). The sac was purplish blue in color. The nature of the hernia was recognized as of the Richter type. The first incision was left open, the abdomen was opened with a left rectus incision, and the gut was reduced following enlargement of the hernia neck. The circulation appeared to return to this small involved portion although a small constriction ring remained. The area was then inverted without interfering with the lumen and the abdomen was closed in layers. The hernia was repaired in the usual anatomical fashion. This patient made an uneventful recovery and is now well, 5 years after operation.

Case 2. An American farmer, 63 years of age, was seen in October, 1930. He stated that several days previous to the examination his bowels had been constipated. A cathartic had not given any results. Two days before he developed a colic-like pain in the epigastrium which was localized just above the umbilicus. This pain was so severe at that time that one-quarter grain of morphine was given. He vomited once on this day. The following day the pain, still localized in the same area, recurred with about the same severity, and again morphine was given. The patient was given an enema with fair result as to the elimination of gas, but it gave him considerable pain. Nausea persisted but there was no further vomiting. No blood or mucus had discharged from the rectum. Six years previously, patient had had an abscess in the right groin which was incised. There had been no recurrence of infection in this area and no swelling had been noticed.

On physical examination patient appeared to be strong, well developed, but to have lost considerable weight. His tongue was dry and clean and his breath was not fæcal. On abdominal examination there was found a moderate general distention but no spasm and no masses. A fluid wave could be demonstrated. There was no visible peristalsis. A small mass about 1 inch in diameter was present in the right femoral region. No impulse was obtained when the patient coughed. No attempt was made to reduce the mass, which was not tender on pressure. A healed scar was noted in this area. Rectal examination was negative. The white blood count was 13,000; the temperature and pulse were normal. A diagnosis of partial intestinal obstruction was made. It was thought that the condition was of malignant origin, probably arising in the colon. At operation

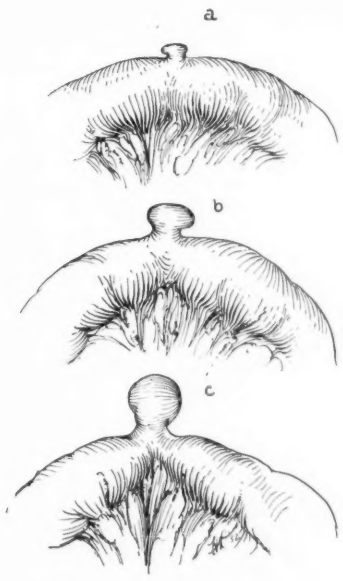

Fig. 1. The size and nature of Richter's hernia of the small intestine are represented diagrammatically. The involved portion of the gut is always on the side opposite the attachment of the mesentery. a, Only a small portion may be involved. If very small no symptoms of obstruction are present, yet gangrene may occur. b, A pouch of this size results in partial intestinal obstruction. c, When over one-half of the bowel circumference is involved an intermittent partial obstruction or complete obstruction may result. This is in agreement with Scarpa's observation that when two-thirds of the intestine is strangulated complete obstruction results.

(Dr. R. B. Cattell) the abdomen was explored and it was noted that the entire large bowel was normal while the small intestine was moderately dilated and thickened. In the right femoral area a portion of the ileum was found strangulated in a small femoral hernia (Fig. 3), of the Richter type, so that the wall of the intestine was firmly engaged but the mesenteric border was free leaving the lumen somewhat narrowed so that it produced an intermittent partial obstruction. The femoral ring was enlarged so that the intestine could be freed. The color returned to the strangulated portion although a circular constriction remained, thus obstructing the lumen to about one-third of its normal caliber. The engaged portion appeared viable. Further inspection of the femoral hernia from within showed that the appendix was firmly engaged beneath the former position of the Richter hernia and was included in and adherent to the sac. In order to free the appendix the sac was inverted and appendectomy was performed. An intra-abdominal repair of the hernia by means of a pursestring suture to obliterate the neck was then done. An enterostomy was then performed 6 inches proximal to the strangulated area of the bowel. The patient's condition remained satisfactory throughout the operation. On the third day after operation he developed severe abdominal pain with a high elevation in temperature followed shortly by death.

Fig. 2. Case 1. The femoral sac has been opened thus exposing the strangulated intestine and showing this to be a hernia of the Richter's type. Laparotomy was done and the hernia reduced.

Fig. 3. Case 2. A loop of terminal ileum is seen partially engaged in a femoral hernia. Partial obstruction is present with the proximal loop of bowel being distended. An outline of the cæcum and appendix is shown with the appendix incarcerated in the femoral hernia beneath the ileum. The previous incision scar in the femoral region is not shown.

These reports show the difficulties of diagnosis. In the first patient there was no evidence of obstruction or of strangulation. We believed that the femoral hernia was the cause of the symptoms; the possibility of a Richter's type of strangulated hernia was not thought of until it was demonstrated at operation. In the second patient an intestinal obstruction was evident but the relation to a possible right femoral hernia was not appreciated until the abdomen was opened. This case is of particular interest in view of the fact that the abscess in the right groin 6 years previously may have been an acute appendicitis. The presence of the appendix in the sac and the dense adhesions may have been factors in the causation of the Richter's hernia. As an inguinal gland was present over the femoral hernia in this patient, it is possible that the abscess may have been related to an adenitis. At operation the strangulated bowel appeared to us to be viable, but undoubtedly the patient died from a peritonitis resulting from the rupture of the strangulated area in spite of the fact that an ileostomy had been done above the obstruction.

In 1906 Burpitt reported the case of a patient with identical findings. In his patient the appendix was present in the right femoral hernia and was non-strangulated but above it there was present a Richter's hernia of the ileum, with strangulation. His patient had had a partial obstruction for a month with acute symptoms of 24 hours' duration. Operation was followed by recovery.

A review of the reported cases reveals common findings. This form of hernia occurs more often in women than in men and only in adults (Rhodes reported a case in a 3 weeks old negro baby, the only exception). The average age is 53 years. The femoral ring is the usual site, this being the region involved in about 90 per cent of the cases. The inguinal region is the next most frequent site; in rare instances, this type of hernia is found in the umbilical, obturator, epigastric and intra-abdominal regions. Richter's hernia is more apt to occur in conjunction with a long standing reducible hernia than with one of recent onset or one that is irreducible. At times no swelling can be felt in the ring although there can usually be seen or palpated a small tumor, varying in size from that of a hickory nut to that of a hen's egg. The terminal ileum is usually the portion of the bowel that is strangulated. Three patients were found in whom the jejunum was involved and one with the colon in the sac. The most common form is one in which the terminal ileum is involved in the right femoral canal. In this form, only a small portion of the circumference of the bowel is involved and rarely is there a complete obstruction (Fig. 1). The outer portion of the bowel away from the mesentery, is always the portion of the

ileum involved so that the general circulation of the bowel is not impaired.

In only one-third of the patients are the symptoms typical of a strangulated hernia with severe obstruction. In the presence of a complete obstruction a mass is usually palpable which is distinctly tender locally and is associated with cramp-like pain in the lower abdomen. Persistent nausea, fæcal vomiting, hyperperistalsis, constipation, together with the general manifestations of shock are the rule in this minority group. At times a persistent diarrhœa is present but rarely is there mucus or melæna present. These patients present such typical pictures of complete intestinal obstruction that operation will be advised early and the results will be fair. While the nature of the cause of the obstruction may not be recognized before operation it will be demonstrated at operation.

By far the majority of the patients (that is, two thirds), however, have mild and indefinite symptoms suggestive of only partial or beginning intestinal obstruction. These are the ones in which only a small portion of the circumference of the bowel is strangulated. It is quite important to recognize such cases early since gangrene and rupture of this portion of the bowel may occur early and the patient may show no serious general response and no evidence of serious obstruction. Fæcal vomiting in these patients is not common, and fair results can be obtained in the elimination of gas and fæcal matter by means of enemas at a time when local gangrene of the gut is present. A mass may or may not be present but if found is of great importance in making a diagnosis. After the first few hours of strangulation local tenderness may be absent and the pain, if present, may be far removed from the point involved. It is in this last group that the operative mortality is very high, since operative interference is usually delayed.

As shown in the reported cases, diagnosis is very difficult; in only 50 per cent could intestinal obstruction be made out. Diagnosis is made difficult also since in only one-half of the reported cases has a palpable mass been present. As our knowledge of this type of hernia increases, diagnosis will be more easily made and the condition more often suspected in patients with femoral hernias presenting symptoms too of partial intestinal obstruction.

The mechanism acting to produce a Richter's hernia is not the same in all cases so that all cases cannot be satisfactorily explained on the same hypothesis. Many times such hernias are associated with old, reducible hernias with adherent bowel and doubtless such adhesions are frequent causative factors. In several instances of Richter's hernia, the case reports show that the hernias have been precipitated by forceful taxis. In addition, the hernia has at times been associated with reduction of a hernia *en masse*. Treves reported 4 such early occurrences. Pearse recently advised against the use of taxis because it may cause reduction *en masse*. From the report of cases it would seem that taxis has caused the production of Richter's hernias in several instances. Pressure produced by a truss over the area of the incarcerated bowel may also contribute to the production of a Richter's hernia. Increased abdominal pressure in the presence of a hernia sac has frequently been described as a possible cause. With an incarcerated segment of bowel, the normal peristaltic waves, in other instances, may well free the major portion of the bowel, leaving a small diverticulum-like portion remaining.

In Richter's hernia the sac is usually small and this factor prevents the engagement of the entire circumference of the bowel. The condition of the strangulated portion of the bowel wall depends on how long strangulation has been present and the size of the neck of the sac. In many of the earlier cases in which gangrene was present subcutaneous rupture led to fæcal fistulæ. In most of these the fistula persisted; in only a rare case did the fistula close spontaneously (Hildanus). Not infrequently the presence of an enlarged tender gland, the result of an inguinal adenitis over the hernia sac, has made it difficult to recognize the underlying condition. Of 38 cases of femoral type hernia, collected by Treves, 7 cases had such enlarged glands of the groin.

TREATMENT

The treatment of Richter's hernia is of course surgical. Operation should be done as soon as possible in order to avoid gangrene. In all cases of intestinal obstruction, either partial or complete, the usual sites for hernia should be palpated. If the diagnosis is made so early that strangulation is not severe and if after observation circulation to the part is shown intact, simple reduction of the involved portion is sufficient. If the strangulated portion is small and has the form of a gangrenous pouch or diverticulum, it may be plicated or turned in without too great reduction in the lumen. This was done in Case 1, reported in this paper. If larger portions of the bowel are involved, resection of the involved loop should be carried out with an end-to-end anastomosis. It is probably advisable to do an enterostomy above the inverted portion or anastomosis to relieve

local pressure, particularly if obstruction has been present.

In the nearly moribund patients two procedures may be carried out. In the first, an enterostomy is done, the gangrenous portion of the gut being left engaged and a local incision made over the hernia as indicated. This plan is suggested by the fact that when a fæcal fistula has formed spontaneously, 30 per cent of the patients recover without operation. In the second plan the involved loop is brought out after the plan of Mikulicz and the fistula is closed when the general condition of the patient has improved. Objections can be raised to either of these methods but they appear to offer the least risk in the more serious cases.

The hernia can be repaired intra-abdominally as has been frequently reported; the sac is inverted and the neck is ligated. Some patients so treated have remained well over a period of years without recurrence. However, the usual anatomical repair either at the time of operation or when the patient is in better condition is the preferred method.

In the cases collected by Treves there was a mortality of 62.2 per cent in those not operated upon. With rare exception all those recovering spontaneously developed persistent fæcal fistulæ. The operative mortality in his group was 56 per cent—4 patients of the operative group having persistent fæcal fistulæ. In Bissell's review of the 20 years preceding 1929, the operative mortality was approximately 22 per cent and none of this recent group had a persistent fæcal fistula. The mortality is much higher in femoral hernia since gangrene is apt to occur more rapidly due to the fact that the neck of the sac is smaller and constriction is more apt to occur.

SUMMARY

Two patients with Richter's hernia are reported. Both occurred in the femoral region and in each instance the terminal ileum was involved. In one the appendix was incarcerated in the femoral sac beneath the engaged intestine.

The majority of these patients do not have complete intestinal obstruction so that strangulation may not be evident. Diagnosis is rarely made before operation. In all cases with symptoms suggestive of partial intestinal obstruction it is important to examine all possible hernia sites.

It seems reasonable to expect a lowering of mortality following operation with the early recognition of partial intestinal obstruction together with a knowledge of this form of hernia.

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A MUSCLE PEDICLE REPAIR OF DEFECTS IN THE PARIETAL PLEURA[1]

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ON the division of thoracic surgery of Harlem Hospital penetrating wounds of the chest due mainly to knives and bullets are of frequent occurrence. We are, therefore, frequently presented with the problem of closing a defect in the parietal pleura rapidly and securely. The defect may be due to the knife of the assailant or to the exploratory incision of the surgeon. It was for the purpose of lessening the time of operation and anæsthesia (and therefore the operative shock) and producing an air tight closure of the thoracic wall that the operation to be described was designed.

Intercostal pleural defects may be repaired by means of pericostal sutures, (as advised by Lilienthal) in which case sutures are passed over the rib above the defect, through the pleural cavity, and under the rib below the defect, and then tied in such a manner as to bring the two ribs together and obliterate the defect. This is an excellent method in cases of incisions made in so-called "interval" thoracic explorations, but it has seldom been applicable in our experience to penetrating wounds because of certain anatomical factors.

Penetrating wounds, particularly stab wounds, may make irregular defects in the chest wall by fracturing the lower, thinner border of the rib, thus leaving a rough edge devoid of intercostal muscle which prevents air tight closure even when the ribs are brought tightly together.

Occasionally a small section of rib or cartilage must be resected in order to reach and ligate a bleeding intercostal or internal mammary vessel which otherwise could not be clamped. This makes an irregular defect.

Stab wounds in the chest occur in our experience almost uniformly in one of these topographical groups:

1. *On the anterior chest wall* within a short distance of the sternum and frequently through the costal cartilages. The victim receives the blow unexpectedly usually on the left side, from a right handed assailant.

2. *Near the lower costal margin* in the anterior axillary region. This blow is received as the victim turns aside and raises his arm to protect himself.

3. *In the back* between the border of the scapula and the spinal column. This blow is generally produced as the victim attempts to escape or to protect instinctively the more vital anterior portion of his body.

An anatomical consideration of these regions will show that near the sternum, at the costal margin anteriorly, and near the spinal column, the ends of the ribs are attached at fixed points and at fixed distances. Because of this fixation attempts at bringing the ribs together by pericostal sutures have been unsuccessful frequently in our experience.

Attempts have been commonly unsuccessful, too, in suturing muscle *over* a defect in parietal pleura. Moreover, in the large triangular area bounded by the borders of the pectoralis major and latissimus dorsi muscles anteriorly and posteriorly, and by the costal margin below, there is little muscle with which to cover a defect. In addition, the intercostal muscles near the sternum contain fewer muscle fibers than the axillary portion or the posterior portion.

In a few cases we have obliterated a defect of parietal pleura by suturing the diaphragm to the parietal pleura, thus plugging the defect and walling off the general pleural cavity. This gives a picture exactly like that found in the first stage of the operation for approaching a subphrenic abscess in which the diaphragm is attached to the parietal pleura. This method has been highly satisfactory in the few cases in which it was used but it has limited use.

In our earlier experience closure of a pleural defect was tedious patchwork which we have been able to obviate by the *use of a muscle pedicle, the free end of which is placed into the pleural cavity, (not on the aperture)* and held in place by suturing it to the structures at the edge of the aperture.

THE OPERATIVE PROCEDURE

The pectoralis major or the latissimus dorsi muscle was employed in all cases except one. (In that case the pectoralis minor was used because the pectoralis major was lacerated and crushed by the assailant who wielded a scissors with the blades held an inch or two apart. The pectoralis minor was severed at its origin and brought down.) The *thickness* of the muscle flap should be made slightly larger than the pleural defect so that it will fit snugly into it. The *length* should be suf-

[1]From the Surgical Service, Harlem Hospital, Dr. John F. Connors, Director.

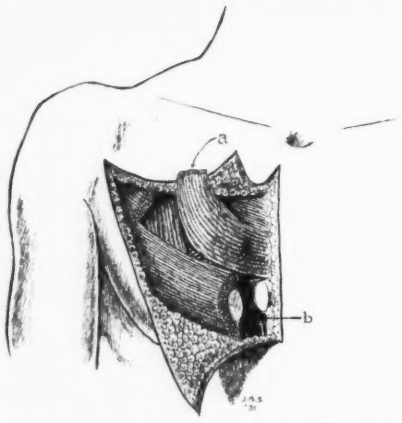

Fig. 1. The muscle pedicle, *a*, severed and lifted from its bed, ready to be inserted into the orifice, *b*, into the pleural cavity. Note that the length of muscle required is longer than apparently necessary to reach the pleural orifice. This is made so because the pedicle contracts considerably after it is severed.

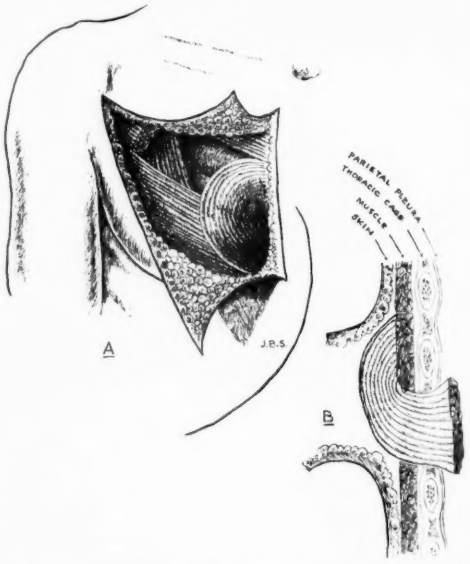

Fig. 2. A. The pedicle has been inserted *into* the orifice. The bed from which the pedicle was taken may be covered by suturing the border of the pectoralis muscle above to the border below. There is no disadvantage, however, in leaving it open. The pedicle is held in place by sutures to the adjacent muscle, fascia ,or periosteum. While the pectoralis major is indicated in these diagrams, the latissimus dorsi may be used in a similar manner. In our experience these two muscles alone were adequate, when made into a pedicle, to reach all pleural defects.

B. This is a cross section of the thoracic wall after the pedicle has been inserted into the defect in the wall. Note the tongue of muscle is well inside the pleural cavity. In one of the cases in which the operation was performed, there was a complication of an infected hæmothorax. Drainage was established at another portion of the chest wall and when the pleural cavity was clean, an investigation was made through the drainage wound of the pleural portion of the muscle pedicle and no abnormality was seen, as granulation tissue covered the area in the same manner in which it covered the remainder of the parietal pleura.

ficient to allow the flap to drop into the pleural cavity for a distance of approximately one inch. No harm will come from too long a flap extending into the pleural cavity, while too short a flap will have a tendency to retract from it. The flap should be cut in such a manner that the base of the pedicle is near the pleural defect and the point of severance of the muscle is distal to it. When we began this method of closure we found that in spite of measurement of the length of muscle apparently necessary for the pedicle flap, we were making too short a flap. This was due to the fact that it contracted after section of the muscle. We overcame this difficulty by increasing the length of the flap so that it was about one and one half times the length apparently necessary. In this way we produced a muscle flap which fitted snugly and without tension. *It is of extraordinary interest to see how such a flap is actually sucked into the pleural cavity* when placed at the orifice of the pleural defect, and how it will be held in place even without suture in ordinary respiration, to be dislodged only in violent respiration or sharp coughing. It serves as a perfect stopper; but should be held in place with a few interrupted sutures or better, a continuous suture attached to adjacent muscle or periosteum. It might also be held *in situ* by the pressure of gauze-packing.

The advantages are not merely speed and efficiency in immediate closure. The same result might be obtained by tight packing with iodoformized gauze. Muscle, however, ordinarily withstands infection well except in cases in which it is crushed with great force as in compound fractures and severe lacerations. Therefore, while we may depend upon gauze or fascia as temporary "stoppers," they may become useless in a short time because of infection and subsequent sucking wounds. One should not hesitate to sacrifice as much pectoralis or latissimus dorsi muscle as necessary to plug the pleural orifice, since the loss of function is not serious. This may be seen frequently in cases of radical amputation of the breast in which the pectoral muscles are removed *in toto*.

We have employed this procedure in 14 cases with failure in only 1. In this instance we used two flaps in the same defect and one of these flaps was macerated muscle. The failure was partial in that the flaps were competent until the fifteenth postoperative day when they separated. By that time, however, the mediastinum had become fixed so that no distress was experienced by the resultant pleural fistula.

The procedure is recommended not only for pleural defects due to penetrating wounds but also for defects following resections involving the parietal pleura. Our experience, however, has been limited to the former type of case.

CORRESPONDENCE

CONGENITAL CYSTIC DISEASE OF THE LUNG

To the Editor: Please permit me to make a belated correction to an article which appeared in SURGERY, GYNECOLOGY AND OBSTETRICS for March, 1931. This article, entitled "Congenital Cystic Disease of the Lung," by Doctor Eloesser, in the discussion of the number of reported cases of congenital cysts of the lung stated that there had been but 4 American cases, "2 of R. T. Miller; a description of an anatomical specimen by Pappenheimer of New York; and 1 of my own."

In 1925, I published (*Bulletin of the Johns Hopkins Hospital*, vol. xxxvii, p. 340) what I thought was the first American case of this condition, and reviewed all previous cases that I could find in the literature. Since then I have discovered that Doctor Pappenheimer, of New York, had published a case in 1912. My reason for overlooking his case was probably due to the fact that it was not published in a medical journal of wide circulation. The other cases mentioned by Doctor Eloesser have been published since the publication of my case in 1925.

Doctor Miller reported only 1 case of congenital cystic lung. The second case he referred to was my own, as a careful reading of his article will show, since he publishes one of my own illustrations illustrating this case. His failure to refer to my article was due, I am sure, to the fact that both his article and mine were in process of preparation at the same time, mine having been published only 2 months before his.

A. R. KOONTZ.

JOHN B. MURPHY

Material is being collected for an authorized biography of Dr. John B. Murphy. If any reader of this JOURNAL has in his possession letters from Dr. Murphy, knowledge of facts concerning his life, or any other data, it would be appreciated if they were sent to the Editors. All material will be returned promptly and the source credited.

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MARCH, 1933

THE REVOLUTION IN THE MANAGEMENT OF PHTHISIS

As recently as 1925 surgical measures were being used for pulmonary tuberculosis by only a few physicians. Today these measures dominate the active treatment of the disease in the leading tuberculosis centers. Although this change has not been brought about by any unique dramatic discovery, it is nevertheless an event of prime interest to the medical world because phthisis is still the leading cause of death between the ages of fifteen and forty-five years.

An era of hope about the curability of progressive cavernous phthisis has succeeded decades of resignation or false optimism on the part of both physicians and patients during the years when the sanatorium regimen was their only weapon. Nevertheless the sanatorium, unaided by surgery, has cured many thousands of patients and as long as tuberculosis exists it will probably remain as the indispensable foundation upon which any active treatment will be built. But the fact must be faced that its greatest independent success is for those patients whose lesions are not extensive and chronic and whose cavities, if present at all, are relatively small and soft walled. The great majority of sanatorium patients belong to the far advanced group in which the death rate without surgery is shockingly high.

The pioneers repeatedly demonstrated during a period of many years that surgery (which term, for convenience, is intended to include induced pneumothorax) offers to a large group of patients with advanced tuberculosis hope in the face of impending disaster and that these patients, contrary to general teaching, withstand expertly performed major thoracic operations remarkably well. Yet the medical profession as a whole refused until relatively recently to accept surgery. This has been due in part to the profession's traditional resistance to any change from therapeutic orthodoxy. This wariness has been accentuated in the case of tuberculosis because of the utter failure of many highly praised "cures." Other contributory factors have been the great emphasis that has long been placed upon the non-therapeutic aspects of laboratory research in tuberculosis, the many ill advised or improperly performed operations that untrained surgeons presented as examples of the surgery of pulmonary tuberculosis and the fact that until recently relatively few competent thoracic surgeons were available.

What resistance to surgery remains is almost wholly passive and is based upon nonfamiliarity with the subject or upon apathy. It is especially to be regretted that many of our largest state and federal sanatoria, which should have taken the lead in offering life-

saving surgery to their wards, have even yet taken no adequate steps to do so.

In a large sanatorium in this country, 66.3 per cent of whose patients have far advanced, and 28.3 per cent moderately advanced, tuberculosis, some form of surgery has been used for 77.1 per cent of all patients admitted with the adult type of pulmonary tuberculosis during a recent eighteen month period. It is interesting that the patients themselves, who are notably close observers of the results of the different operations used for their fellow patients, rarely reject any recommendation for surgery.

The many operations now available afford great flexibility in the choice of the procedure or combination and sequence of procedures that is most likely both to heal the lesion and to conserve maximum function. Certain patients for whom temporary or permanent phrenic nerve interruption and pneumothorax have been tried and failed, present suitable indications for closed or open intrapleural pneumolysis; oleothorax; extrapleural pneumolysis with paraffin, pectoral muscle, gauze, or rubber bag filling; scaleniectomy; temporary or permanent intercostal nerve interruption partial thoracoplasty; or some combination of these operations, and may thereby be saved from the necessity of having the more dangerous total thoracoplasty.

Total thoracoplasty is, however, indispensable for selected cases in which much of one lung is actually destroyed. A restricted thoracoplasty often fails to close a cavity and a persisting partially open cavity remains a lesion of grave ultimate significance, no matter what gratifying general improvement the patient may have made after operation. A restricted thoracoplasty which fails to close the cavity is a radical and not a conservative measure because a patient who is subjected to the risks that are common to any thoracoplasty should receive the full benefits to which those risks entitle him. Fortunately, it has been found that a very extensive thoracoplasty in three, four or more stages, is as safe, and certainly much more effective, than the restricted one or two stage thoracoplasty that is still too often used. There are two clinics, which happen to be known to the writer, in which, during the past eighteen months among a total of one hundred and eleven consecutive patients, representing two hundred and ninety-nine major operations, there have been only two deaths during the first postoperative month and six deaths thereafter. These patients do not represent a group in which only those with ideal indications for thoracoplasty were included and with doubtful indications excluded; among them were many patients with a poor operative prognosis, but a hopeless one without operation.

The modern sequence of measures used in the management of pure tuberculous and mixed tuberculous and pyogenic empyema has vastly improved the results and has dissipated much of the former utter pessimism about the curability of this dreaded disease.

The balanced judgment of the combined medical and surgical points of view is necessary to control undue enthusiasm or timidity and for the selection of the best possible operation for the individual patient. A surgeon's experience with phthisis may not have been sufficiently broad to entitle him to express himself with authority as to what operation is best for the particular patient. On the other hand, the mere fact that an internist may be a specialist in tuberculosis and thoroughly familiar with the history of his patient does not necessarily qualify him to pass expert judgment in matters of surgical therapy, if his experience with it has been limited.

The subject as a whole is complex and the margin between safety and danger and be-

tween cure and mere improvement is narrow. In many countries an increasing number of medically-minded surgeons and, occasionally, surgically-minded internists are apprenticing themselves to active thoracic surgical clinics in preparation for the competent practice of thoracic surgery as a specialty. The medical profession has finally accepted the contributions of surgery as the most hopeful and successful advance that has been made in the treatment of pulmonary tuberculosis since the sanatorium idea was introduced fifty years ago.

JOHN ALEXANDER.

PEPTIC ULCER

"CURES," or treatments, of peptic ulcer have been numerous; usually introduced with enthusiasm that soon subsides, to be followed by various modifications and gradually pass into disuse; to be repeated with another method.

One explanation of this phenomenon may be found in a study of the natural history of untreated cases, which shows peptic ulcer to be a chronic disease, with the ulcer as a striking local manifestation characterized by cycles of recurrences and remissions but with a natural tendency toward repair.

Treatment, to be rational, should be based upon etiology. The possibility of hydrochloric acid, because of its constant presence, acting as an important etiological factor, has been recognized by many, notably and recently by Matthews and Dragstedt. This relationship may be emphasized by a consideration of ileal ulcers adjacent to Meckel's diverticula that contain gastric mucosa.

Treatment striving to neutralize hydrochloric acid after its secretion has not been very successful, and therefore an attempt at minimizing its secretion has been offered as an improvement. Proper treatment may well be multiple, with efforts being exerted in four directions, namely:

1. Co-operation of the patient (much has been said about the advisability of co-operation between the internist, radiologist, and surgeon; but of more importance is a change in the patient's attitude from that of a miracle searcher to that of a co-operator with the physician). The methods of education so successful in the management of diabetes might well be imitated in peptic ulcer.

2. Social and economic readjustments will usually be necessary preliminaries in securing the essential factor of *rest* (physical and psychic.

3. Medical or non-operative management includes: antispasmodics, alkalies or antacids, emollients, and various miscellaneous measures that are often followed by symptomatic relief which may, with difficulty, be differentiated from the remissions which characterize the disease. In this connection the statement of Ryle may be repeated: "We should be interested in peptic ulcer the disease and not peptic ulcer the lesion."

Diets are numerous, frequently conflict in theory, but are followed by a strikingly similar percentage of favorable results. Dietotherapy should aim not only to neutralize hydrochloric acid already secreted, but should also aim to diminish its secretion, and should precede and follow all surgical measures.

"It is not possible, as yet, to describe in detail the mechanism of hydrochloric secretion. All of the mechanisms suggested depend upon selective membrane properties. . . . There can be no doubt that the blood base chlorides are the raw materials for gastric hydrochloric acid and that a mechanism exists for converting these simple chlorides into hydrochloric acid, which diffuses outward into the stomach (free or combined) while the basic component diffuses in the opposite di-

rection into the blood stream. The phenomenon of 'alkaline tide' is as authentic as is the presence of hydrochloric acid in gastric juice."

If this quotation from Bradley is granted, then a salt free, or salt low, diet is plainly indicated, in an effort to decrease the reserve and, in turn, the available chloride that might unite with hydrogen to form hydrochloric acid. Such a diet has been utilized in cardio-vascular-renal diseases, epilepsy, tuberculosis, and in peptic ulcer by Krantz and Silver.

4. Surgical. The indications for operative measures may, at the present time, be outlined as follows: with acute ulcer, perforation calls for surgery; hæmorrhage for non-operative management; with chronic ulcer, non-operative measures may be given a number of trials in duodenal ulcer, but because of malignant potentialities prompt surgical measures may be advisable in gastric ulcer.

The usual operative procedures such as resection (which removes the effect and allows the cause to remain) and pyloroplastics or gastro-enterostomies (which destroy or nullify the pyloric mechanism) are frequently followed by return of symptoms, and sometimes secondary ulcer.

Indirect methods such as vagotomy, adrenal denervation, partial devascularization, radiotherapy, physiotherapy, psychotherapy, protein shock, and many other types of therapy have been recommended.

The physiological fact that the fundus secretes acid and the antrum alkali, has not, until recently, been applied in treatment. With repeated operations for recurrent ulcers one finds more satisfactory results, as more and more of the fundus has been removed, and it seems more rational to remove the cause (the acid) than to remove the effect (the ulcer) and allow the cause to remain.

A direct method of diminishing the secretion of hydrochloric acid by minimizing the area capable of such function (the fundus) as a primary, and not a second or third, operation, and especially applicable in cases of jejunal ulcer has been carried out by Connell and is now on clinical trial.

By so doing, the lesser curvature, the *Magenstrasse*, an important factor in motility, is retained; and the pylorus, with its antro-pyloro-duodeno- neuromuscular mechanism, so essential in local neutralization and in maintaining general acid base equilibrium, is not sacrificed.

Fundusectomy is offered as a compromise between gastro-enterostomy, which by some is considered too conservative, and gastrectomy, which by many is considered too radical. It also complies with the very fair requirement of Balfour that "it should not interfere with future surgical treatment, should ulcer develop subsequently."

GREGORY CONNELL.

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EARLY AMERICAN MEDICAL SCHOOLS

ALBANY MEDICAL COLLEGE
MEDICAL DEPARTMENT OF UNION UNIVERSITY

Its Founding and Development

A. HAZEL CURRY, M.D., Albany, New York
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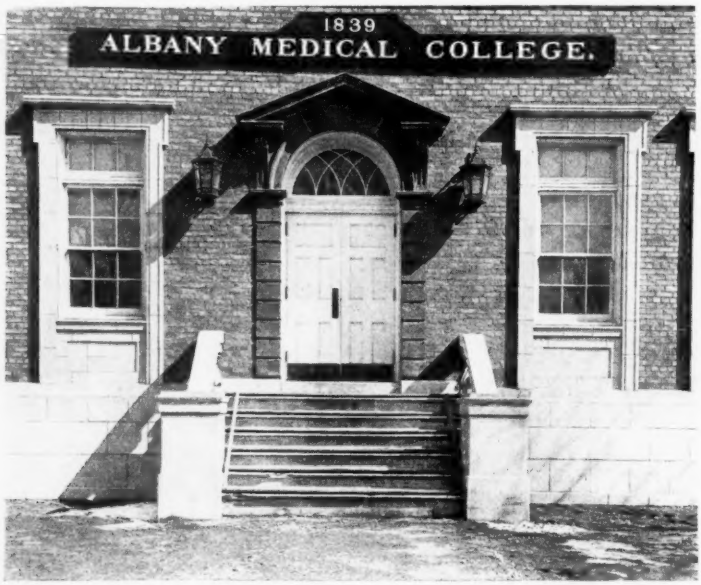
THE Albany Medical College owes its existence to the eighteen years of ceaseless perseverance of Dr. Alden March. A lecture delivered by Dr. March, January 11, 1830, "On the Expediency of Establishing a Medical College and Hospital in the City of Albany" reveals the fact that he had conducted private courses of medical instruction since November, 1821. The new college was organized in 1838 and formally opened January 2, 1839. It was incorporated by the New York State Legislature, February 16, and graduated its first class on April 24, of the same year, the thirteen members having completed their course in four months. Today this institution is the second oldest surviving medical college in the state as only one of the three which antedated its inception is now in existence.

Although Dr. March had hoped for a "practical school of medicine, such as is afforded by a well regulated hospital" (2), the Albany Hospital was not opened until 1851. "The objects of the corporation set down in the by-laws at that time read as follows:

"1. To provide philanthropy by the establishment within the city of a hospital and dispensaries to furnish medical and surgical aid and trained nursing to sick and injured persons.

"2. To promote medical education by maintain-



The original doorway as it appears in the new building.

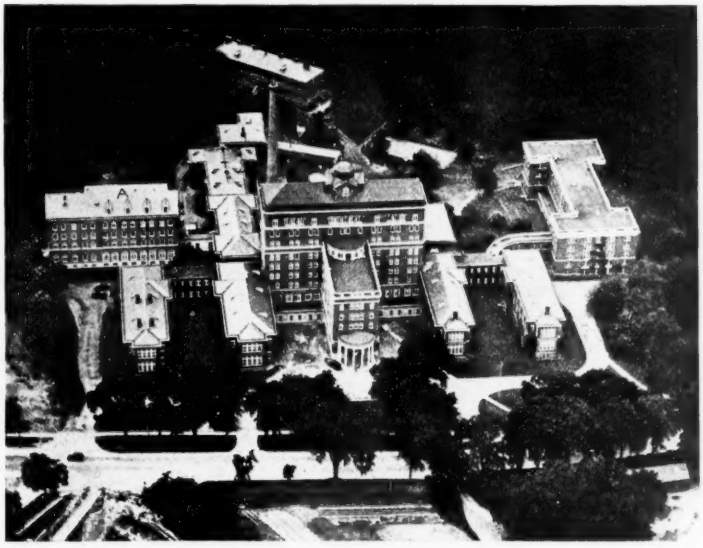
ing a school of instruction in the science and art of medical and surgical nursing and by offering opportunity for clinical and laboratory instruction to medical students." (1)

Despite the lack of hospital facilities in the first years of the medical school, practicability as the basic principle of Dr. March's pedagogy was evidenced in his clinical presentations. "On the first Saturday of the term, Dr. March inaugurated his surgical clinics, held in the college and at which he presented a large number of cases requiring operation or treatment, and this new feature in medical education which he introduced soon came to be generally adopted by medical schools throughout the country" (6).

The first president of the faculty was Dr. March who served in this capacity from 1839 to his death in 1869, a period of thirty years. This remarkable physician and surgeon thus gave nearly fifty years of his life to the founding and development of the Albany Medical College and Albany Hospital. His successors have been Dr. James McNaughton until his death in 1874; Dr. James Armsby until his death in 1875. At this time the title of president of the faculty was changed to that of dean. Dr. Thomas Hun served as dean until his death in 1896; Dr. Albert Vander Veer to 1904; Dr. Samuel B. Ward to 1914; Dr. Willis Tucker to 1915; and since then Dr. Thomas Ordway, under whose administration the new Albany Medical College has been built and the Albany Hospital reconstructed.

In 1873 the Albany Medical College became a unit of Union College "retaining, however, its own name, its own trustees, and its hitherto existing corporate rights. In 1915 the college was reorganized for teaching on a university basis" (5). In 1927 the Albany Medical College and Albany Hospital became legally united by the formation of a Joint Administrative Board to function as a hospital medical college, thereby promoting medical education and affording more effective treatment of patients.

The indefatigable labor of Dr. March a century ago to establish this institution is a tradition of patience, research, and careful planning which has been followed faithfully throughout the ensuing years. This policy has brought to the school recognition for reliability and dependability. The constantly increasing service of the Albany Medical College is evidenced in one of its latest developments—its Regional Extension Department. By means of this regional work, it maintains contacts with physicians throughout a wide rural area, affording them opportunities for acquiring knowledge of the newer developments in medicine, and strives to make medical service accessible to all communities. In aiding graduates to keep abreast of the new medical and surgical achievements, as well as in the teaching of under-



Aeroplane view of Albany Medical College buildings.

graduates, the Albany Medical College holds to the ideals of the founder: "The value of our pursuits . . . can be estimated only by the value of life itself, and of that which alone endears it to its possessor—health. The enlightened and judicious practitioner of medicine is justly ranked among the benefactors of mankind. In proportion as his time and talents are employed in acquiring an accurate and extended knowledge of his profession, in the same proportion will he become useful to his fellow citizens, and be entitled to their approbation and support. He should not be devoted to the mere sordid accumulation of wealth. A more noble, generous, and humane motive should hold the first place in his sentiments and actions. Prevent and relieve human misery, should be his motto, engraven in indelible characters on the tablet of his heart" (3).

BUILDINGS OF ALBANY MEDICAL COLLEGE

During its existence of more than ninety years, the Albany Medical College has had two homes: its present one on University Heights, New Scotland Avenue, and its first one on Eagle Street, between Jay and Lancaster Streets. The latter was originally the Lancaster School building which was completed in 1817, having been designed by Philip Hooker, a noted architect of his time. With the passing of the Lancasterian monitorial system of teaching, the Common Council of the City of Albany voted, March 28, 1836, to close the doors of the school. Dr. March, ever alert, saw the opportunity to secure this place for his proposed medical college and applied to the Common Council for the building for such purpose "in the event of a charter being granted by the legislature" (4). Finally, April 16, 1838, the Common Council voted to lease the property to the trustees of the Medical College for five years, rent free, the petitioners having agreed to repair the already dilapidated building and to surrender it in good condition at the end of the term specified.

The new building, modern and capacious, is in direct continuity with the Albany Hospital and in close proximity to the School of Pharmacy, the Albany Law School and the Dudley Observatory, all units of Union University, the New York State Laboratory and the Bender Laboratory. In addition to its own library the medical college has access, through its courier system, to the reference books in the New York State Medical Library, the nucleus of which was formed by books given to the state by the college in 1890.

In the new building the original doorway still stands: the white marble threshold, worn by years of service, has echoed and re-echoed the firm, determined footstep of the founder as he entered to open the Albany Medical College on the second day of January, 1839. The two colonial fireplaces, one in the library and the other in the trustees' room, memorialize years of progress which have made possible the Albany Medical College and Albany Hospital of today.

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THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE human breast, an organ with a peculiar anatomical construction, is, during a considerable period of life, subjected to various stimuli. It responds to these stimuli, be they physiological or otherwise, in a manner which is unique and at times mysterious. The superficial location of the breast makes for relatively prompt recognition of anatomical and functional abnormalities. Groups of these abnormalities, whether physiological or pathological, have been recognized and described; however, there is in the mind of most medical men, a sense of confusion relative to these conditions—one need mention only the term "chronic mastitis" and place it in the category of "rheumatism" and like terms. An analysis of the situation immediately suggests the reason for this confusion, namely the lack of concerted study for a sufficient period of time to justify an opinion.

The work[1] of Cheatle and Cutler is, therefore, a most welcome and satisfying contribution to the subject of breast pathology. Their conclusions are the result of some thirty-five years of continuous clinical and microscopical study of the breast, based upon a definitely established theory and verified by numerous serial sections of the entire breast. For the first time, there is established a principle of breast pathology which is clear and concise and which is proved by ample concrete evidence.

The authors divide epithelial growths into two types of desquamative hyperplasia—mazoplasia and the cystiphorous—and neoplasia. The term "chronic mastitis" and "chronic cystic mastitis," as they appear in the literature, include under their description states of the breast which are more physiological than pathological and also states which are distinctly pathological (cysts and papillomata). These states differ from each other in their etiology, prognosis, and treatment so that it is of importance to separate them. The authors have isolated that condition which appears to be more physiological than pathological and describe it under the term of mazoplasia.

Mazoplasia is that condition in which there is a type of desquamation of the epithelial cells in the terminal ducts and their acini with hyperplasia of the pericanalicular and periacinous connective tissue and often with new formation of ducts and acini. The shed epithelium, which consists of cells which are irregular, stain poorly and are in a state of degeneration, may distend the ducts and acini, giving rise to diffuse pain and, if the breast is not too fat, a generalized fine nodularity, which can be felt upon palpation. Cysts do not belong to this state but are associated with an entirely separate and distinct pathological process. In the normal breasts of all women who have borne children mazoplasia is almost universally present in some degree until the menopause and the only pathological state that can be directly traced to it is the formation of fibroadenomata.

Cystiphorous desquamative epithelial hyperplasia is that type of hyperplasia which ends in the formation of cysts. It is entirely different in its biology and morphological appearances to that of mazoplasia although the two may coexist. In mazoplasia the type of epithelium remains stable and forms neither cysts nor papillomata; moreover, the acini never coalesce. In the cystiphorous type, the epithelial hyperplasia may undergo a radical change into epithelial neoplasia, the change being traceable morphologically in all stages of transformation. About 20 per cent of all cases of carcinoma of the breast can be definitely traced to begin within the lesions of the cystiphorous state, the supervention occurring in the late fourth and early fifth decade and requires a period of about thirty years to culminate. The authors have shown that the process may become arrested in the decade of cyst production, in others it may stop at the decade of benign neoplasia (papilloma) from which state it may pass into the decade of malignant neoplasia (carcinoma). This fact makes the lesion one of great menace and immense portent.

The authors believe that papillomata are much more common than is generally supposed. By a study of whole microscopical sections of the breast, they have been able to demonstrate their presence when not in the least suspected; moreover they have shown that papillomata are generally multiple, as many as 150 tumors having been counted in one microscopical section of the whole gland.

In a discussion of neoplasia, there is an interesting description of tumor formation and the association of carcinoma with pre-existing epithelial neoplasia. The authors stress the importance of staining the elastica in studying and interpreting morphological appearances. The problems encountered in carcinoma, Paget's disease of the nipple and benign tumors are expounded in a meticulous manner. There is included a chapter on radiation treatment of carcinoma of the breast. The authors conclude that

[1] TUMOURS OF THE BREAST; THEIR PATHOLOGY, SYMPTOMS, DIAGNOSIS, AND TREATMENT. By Sir. G. Lenthal Cheatle, K.C.B., C.V.O., F.R.C.S., and Max Cutler, B.Sc., M.D. Philadelphia and Montreal: J. B. Lippincott Company, 1931.

since the reported percentage of "cures" of mammary carcinoma by operation alone vary within such wide limits, it can hardly be expected that the value of radiation can be determined by comparative means. They report some statistical studies but state that several years must elapse before sufficient and accurate data are available. The authors favor the use of pre-operative radiation in selected cases and postoperative radiation in moderate repeated doses.

This work which is clarified by 18 colored plates and 468 illustrations all original, is indeed a masterpiece. It represents the untiring efforts of many years of progressive and thoughtful study based upon a workable hypothesis relative to tumor formation in the breast. J. A. WOLFER.

ATLASES of obstetric roentgenology have been wanted ever since the earliest days of the use of the X-rays, for one of the first applications of X-ray diagnostic methods was to the female pelvis and to the fetus. But because of mechanical and technical difficulties only within recent years has it been within the power of the radiologist to produce roentgenograms of the fetus *in utero matris* which from the photographic standpoint could be utilized for publication purposes. Ordinarily the extremely contrasty roentgen films, although rich in detail of both maternal and fetal parts and serving excellently for diagnostic purposes, could not be reproduced photographically and on the printed page without great loss of detail. These difficulties still exist to a certain extent, but by improvements in the apparatus and technique of roentgenology and by bringing to the obstetrical clinic the artifices of the professional photographer in retouching negatives, it has been possible for Liepmann and Danelius to publish their beautifully printed and illustrated atlas.[1]

The authors discuss the development of obstetrical roentgenology, the normal position of the fetus, the various changes which may occur, and the forces and factors which may bring them about, varieties of pelvic deformities, spontaneous changes in the position of the fetus, a long series of observations on the mechanism of birth, a discussion of the unusual and pathological positions of the fetus, pelvic and fetal mensuration, deformities and monstrosities, intra-uterine fetal death, and other pertinent questions relating to obstetrics in which the roentgenograms throw light or assist in illustrating. Most of the roentgenograms are accompanied by line drawings which clarify the interpretations. The volume is a valuable contribution to roentgenology and to obstetrics and will undoubtedly be regarded as a classic. JAMES T. CASE.

IN a compact volume Jacobson has succeeded in making available to medical students and practitioners, a comprehensive, concise and readable discussion of the subject of clinical mycology.[2]

There are ten chapters, entire chapters being devoted to dermatomycosis, moniliasis, maduromycosis, sporotrichosis, blastomycosis, actinomycosis, coccidioides, torulosis, and aspergillosis. The history of each disease is first discussed, then the etiology, mycology, clinical manifestations, pathology, diagnosis, and finally the treatment. Each subject is very thoroughly covered, and there is a complete bibliography with each chapter.

The illustrations are for the most part very good, the print and paper excellent. The book reads well, and should prove to be of great service to the dermatologist, internist, and general practitioner.

EDWARD A. OLIVER.

THIS work[3] on the individuality of the blood by Professor Lattes, first appeared in Italian in 1923, in German 1925, in French 1929, and now in English. It has been revised and enlarged until at present it consists of 413 pages of general review of the subject and citation of the work of leading students in the field. The author crystallizes the various data, opinions, and methods into a very readable volume. The bibliography of the book is extensive (91 pages).

Attention is concentrated on those constitutional peculiarities of the blood which enable us to distinguish between individuals of the same species. This is what is meant by "individuality" of the blood with which this book is alone concerned. These individual characteristics have not been demonstrated by morphology or chemistry but almost entirely by serology.

The hereditability of the blood characteristics caused v.Dugern and Hirszfeld to state that "the bio-chemical structures of A and B corpuscles never make their appearance in the offspring unless they are present in one or both of the parents." If parents contain "peculiar structure," it will be found as a rule in their children. The transmission of the blood groups takes place according to Mendel's law and the iso-agglutinable properties A and B behave as dominants, but they are affected by 2 allelomorphic characters, one being derived from each parent, the combination of which give rise to 6 genotypical blood groups. These findings bear out Mendel's laws of heredity in man. Much data are presented on the individuality of the blood as an ethno-anthropological fact. It is clear that the study of the blood groups made go far in solving the origin of races of men. These same principles are becoming well established in forensic medicine to establish the parents of children. Thirty-four pages are given to technique of

[1] GEBURTSHILFER UND RÖNTGENBILD: ERWEITERUNG UND ERNEUERUNG DER GEBURTSHILFE DURCH DIE RÖNTGENDIAGNOSTIK. By Universität-professor Dr. Wilhelm Liepmann, and Dr. Gerhard Danelius. Berlin and Vienna: Urban & Schwarzenberg, 1932.

[2] FUNGOUS DISEASES; A CLINICO-MYCOLOGICAL TEXT. By Harry P. Jacobson, M.D. With Introductions by Jay Frank Schamberg, M.D., and Howard Morrow, M.D. Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1932.

[3] INDIVIDUALITY OF THE BLOOD IN BIOLOGY AND IN CLINICAL AND FORENSIC MEDICINE. By Prof. Leone Lattes. Translated by L. W. Howard Bertie, M.A., B.M., B.Ch. (Oxon.). London: Oxford University Press, 1932.

using the points discussed in this book. One section of the volume is given to blood transfusions.

M. H. BARKER.

A BOOK[1] which is just what the name implies—a clinical study of endocrinology has been written by Mazer and Goldstein who are essentially clinicians. The presentation therefore follows the natural clinical sequence of events. The functional phases are taken up in their normal order—puberty, menstruation, pregnancy, lactation, and the menopause. The latent and newest thoughts in endocrinology are fully expressed and a rather considerable portion of this monograph is devoted to therapy. It is this portion of the work, if any, which one feels tempted to criticize adversely. Endocrinology is not at present a completed study and endocrine therapy is still in its infancy. Much careful and intensive work must be done before final statements may be made. The authors show a tendency to be dogmatic. "The administration of anterior pituitary sex hormone is almost a specific in the treatment of functional uterine bleeding of puberty and maturity." This phase of gynecological practice would be greatly simplified if such were the case.

The monograph is well illustrated. It ends with a bibliography of 649 articles on the subject and is most worth while as a handy and useable reference work on endocrinology in the female, gathering together as it does the voluminous literature on the subject. In addition it presents the personal contributions of the authors. These are considerable and lend to the work a most intimate and attractive style. It is a monograph well worth the reading.

RALPH A. REIS.

FOR various reasons, the book[2] by Doll and his collaborators on *Mental Deficiency due to Injuries* is valuable. To some extent it supplies information of unquestioned validity. It emphasizes the challenge already repeatedly made by others, that obstetricians should make persistent efforts to discover methods by which the incidence of birth injury can be reduced.

The most important contribution, however, is the evidence that careful, resourceful study of individuals suffering from cerebral palsy, by psychologists and orthopedists, reveal possibilities unsuspected by less thorough methods. Obviously the attitude that "among birth injured subjects we have a kind of natural experiment in neurophysiology for studying the relation of behavior to cerebral integrity" is both correct and stimulating. Dr. Doll and his co-workers properly and fortunately regard this volume as a preliminary report. As such it has great value and interest.

BRONSON CROTHERS.

AS described in the title, Bertwistle's *Atlas*[3] a collection of 767 reproductions of positive prints from roentgenograms, including examples of most of the pathological lesions ordinarily encountered. Each roentgenogram is accompanied by a few lines of text and sometimes by a descriptive outline drawing. Often the text seems inadequate to illuminate the illustrations, considering the author's intention to provide a working guide for the clinician who, without being specially concerned with the technical side, yet desires to know what radiology is capable of revealing to him. It is thought that the presentation of a number of plates with descriptions and clinical notes will enable him to realize which cases are suitable for this form of examination. An interesting chapter concerns milestones in roentgen diagnosis, in which the author lists some of the outstanding innovations of each year in the development of radiology.

An unusual style is used for preparing the roentgenographic illustrations as silhouettes. The outline of the soft tissues is scratched in with a needle and a print made, after which the silhouette is completed by filling in the background with India ink.

A serviceable atlas for the general practitioner and for the novice in radiology.

JAMES T. CASE.

THE monograph by Hartmann and Bérard, discusses all phases of cancer of the tongue.[4] Following an introductory chapter on the surgical anatomy of the tongue, the author presents an interesting historical review describing the development of our knowledge upon this subject. During the first period (1760) the tongue was looked upon as an object of religious respect because of the function of speech. During the second period (1850) attempts were made to overcome difficulties in operative technique. The third period (1880) was characterized by advances in the knowledge of pathological anatomy. It was during this period that simultaneous ligation of both lingual arteries was performed as treatment for cancer of the tongue. This procedure was followed by diminution in the size of the tumor. During the fourth period (1890) massive ligature was abandoned and leucoplakia was first recognized as a precancerous lesion (Trelat). The most important advance in technique consisted in hæmostases effected by ligation of the lingual and external carotid arteries. The fifth period (1920) was marked by a recognition of the importance of block dissection of the neck, and it was during this period that the necessity for external removal of the cervical lymphatic glands secondary to cancer of the tongue was fully established. The sixth period is characterized by progress in the radiation treatment of this condition.

[1] CLINICAL ENDOCRINOLOGY OF THE FEMALE. By Charles Mazer, M.D., F.A.C.S., and Leopold Goldstein, M.D. Philadelphia and London: W. B. Saunders Company, 1932.

[2] MENTAL DEFICIENCY DUE TO BIRTH INJURIES. By Edgar A. Doll, Ph.D., Winthrop M. Phelps, M.D., and Ruth Taylor Melcher, M.A. New York: The Macmillan Company, 1932.

[3] A DESCRIPTIVE ATLAS OF RADIOGRAPHS; AN AID TO MODERN CLINICAL METHODS. By A. P. Bertwistle, M.B., Ch.B., F.R.C.S. (Ed.). 2d ed. rev. and enl. St. Louis: The C. V. Mosby Company, 1932.

[4] BIBLIOTHÈQUE DU CANCER. Professors H. Hartmann and L. Bérard, Directeurs. Dr. A. Chalier, Secrétaire. CANCER DE LA LANGUE. By Pierre Sebileau. Paris: Gaston Doin & Cie, 1932.

The author emphasizes the important rôle of syphilis in the development of cancer of the tongue. He correctly warns against the use of caustics such as chromic acid, silver nitrate, and the thermogalvanic cautery in the treatment of leucoplakia, stating that these methods constitute the easiest manner of hastening the transformation of leucoplakia to carcinoma.

Chapters upon the gross anatomy, microscopical structure, and clinical cause of the disease are complete, clearly presented, and well illustrated.

Surgical excision is advised for the accessible lesions and radium insertion for those less accessible. Complete removal of the cervical lymphatic glands is advised when there is clinical evidence of disease. The technique of radium and X-rays in the treatment of cancer of the tongue is described.

This treatise is a useful résumé of the subject clearly presented by a writer who evidently has had considerable experience with the disease. Some radiotherapists will differ with the author upon the wisdom of performing surgical excision of any carcinoma in the tongue regardless of its location. At the Curie Institute, for example, radium is the exclusive method even when the lesion involves the most accessible portions. MAX CUTLER.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

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ANNUAL CLINICAL REPORT OF THE GOVERNMENT HOSPITAL FOR WOMEN AND CHILDREN, EGMORE, MADRAS, FOR THE YEAR 1931. Madras: Superintendent, Government Press, 1932.

BETTERMENT OF LIFE INSURANCE SERVICE. PROCEEDINGS OF THE TWENTY-SIXTH ANNUAL CONVENTION OF THE ASSOCIATION OF LIFE INSURANCE PRESIDENTS HELD IN THE WALDORF-ASTORIA. New York, 1932.

EVERYDAY PRACTICE SERIES. Edited by Harlow Brooks, M.D. OFFICE SURGERY. By Fenwick Beekman, M.D. Philadelphia and London: J. B. Lippincott Company, 1932.

A TEXTBOOK OF SURGERY. By John Homans, M.D. 2d ed. Springfield, Illinois and Baltimore, Maryland, Charles C. Thomas, 1932.

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THE PRACTITIONERS LIBRARY OF MEDICINE AND SURGERY. Volume iii. PRACTICE OF MEDICINE. New York and London: D. Appleton and Company, 1933.

PICTORIAL MIDWIFERY. By Comyns Berkeley, M.A., M.C., M.D. Cantab., F.R.C.P.Lond., F.R.C.S.Eng., F.C.O.G. Illustrated by Georges M. Dupuy, M.D. 2d ed. New York: William Wood and Company, 1932.

DIE SCHWANGERSCHAFTSDIAGNOSE AUS DEM HARNE: PRAKTISCHE UND WISSENSCHAFTLICHE ERGEBNISSE. By Dr. S. Aschheim. 2d thor. rev. ed. Berlin: S. Karger, 1933.

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LE GENOU; ANATOMIE CHIRURGICALE ET RADIOGRAPHIQUE CHIRURGIE OPÉRATOIRE. By Antoine Basset. Paris: Masson et Cie, 1932.

MORRIS' HUMAN ANATOMY; A COMPLETE SYSTEMATIC TREATISE. Edited by C. M. Jackson, M.S., M.D., LL.D. 9th ed. Philadelphia: P. Blakiston's Son & Co., 1933.